Review Article

Multiple Chemical Sensitivity and Idiopathic Environmental Intolerance (Part One)

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Abstract

Multiple chemical sensitivity/idiopathic environmental intolerance (MCS/IEI) is a commonly used diagnostic term for a group of symptoms. These symptoms have been described and commented on for more than 15 years in the USA. Recently, it has also been observed in Japan. The main features of this syndrome are multiple symptoms involving in multiple organ systems that are precipitated by a variety of chemical substances with relapses and exacerbation under certain conditions when exposed to very low levels which do not affect the population at large. There are no laboratory markers or specific investigative findings. Although traditional medical organizations have not agreed on a definition for this syndrome due to the lack of obvious evidence to demonstrate the existence of these symptoms, it is being increasingly recognized. It constitutes an increasing percentage of the caseload at occupational/environmental medical clinics.

Part one of this review article discusses pathophysiological theories, substances which cause symptoms, prevalence in the general and specific populations, past history and family history, and clinical symptoms of MCS/IEI patients.

Key words: multiple chemical sensitivity, idiopathic environmental intolerance, chemical intolerance, pathophysiological theories, clinical symptoms

Introduction

Multiple Chemical Sensitivity (MCS) refers to the condition in which people report negative symptoms in response to exposure to common chemicals, and attribute their sensitivities to prior exposure to the same or often structurally unrelated chemicals. The onset of MCS is often attributed to prior repeated chemical exposure in the home and/or workplace, and once initiated, symptoms are triggered by extremely low levels of many chemicals or types of food. Symptoms reportedly differ in focus and intensity depending upon the type or duration of exposure, but share the characteristics of disabling and limiting the person’s access to areas where such exposure might occur.

At a World Health Organization-sponsored conference in 1996 (1), conferees urged that research continue concerning MCS while conceding that its validity has not been established. They proposed the term “idiopathic environmental intolerance (IEI)”, because many people with MCS were suggested to develop symptoms in response to environmental agents, such as electromagnetic waves, other than chemicals. For this reason, we will henceforth refer to this disorder as MCS/IEI.

The first case involving a patient with multiple, disabling chemical intolerance was described nearly half a century ago (2). First described in 1952, the syndrome has engendered over 20 names, including environmental illness, total allergy syndrome, 20th century disease, and chemical AIDS (3). Originally called “the petrochemical problem,” this condition has been the subject of several sponsored meetings and professional conferences over the past 10 years (4). Chemical intolerance or chemical sensitivity poses major scientific and policy challenges for physicians, toxicologists, ecologists, employers, building owners, chemical producers, and government officials. Investigators in more than a dozen countries have reported cases arising in diverse demographic groups following exposure to indoor air contaminants, chemical spills, industrial chemicals, and pesticides (4).

Despite the work and dedicated investigations of many researchers, there is no widely accepted definition of MCS/IEI because there is very little agreement on what the symptoms represent. These aspects of MCS/IEI have led some observers as well as scientific policy committees to reject MCS/IEI as an organic disease (5). Although MCS/IEI is not generally accepted by mainstream medicine (6, 7), and the Scientific Council of the American Medical Association (8) urged that it not be recognized, a growing body of literature (9–11) has documented many people
in the United States and elsewhere who have developed a set of symptoms that they and some physicians attribute to chemical exposure. In the present paper, we discuss pathophysiological theories, substances which cause symptoms, prevalence in the general and specific populations, past history and family history, and clinical symptoms of MCS/IEI patients.

The differences between chemical intolerance (sensitivity) and MCS/IEI

Since there are many diagnostic names related to chemical intolerance and chemical sensitivity other than MCS/IEI, symptoms of MCS/IEI should be differentiated from chemical intolerance and chemical sensitivity. As for the differences between MCS/IEI and chemical sensitivity, Davidoff and Keyl (12) observed that certain members of the general population have reported mild sensitivity to chemicals. However, these people with mild sensitivity differ from the MCS/IEI groups with respect to the number and types of symptoms reported, the duration and frequency of response, and associated features. Kutsogiannis and Davidoff (13) also observed that MCS/IEI syndrome was significantly different from manifestations of chemical sensitivity in a sensitive clinical control. Furthermore, in contrast to sensitive controls, MCS/IEI patients reported more illnesses from more common types of environmental chemical exposure, more changed tolerances, longer recovery time after illness-inducing exposure, more odor related symptoms (including odor intolerance), longer time of illness related to chemical exposure, and more symptoms, especially of the following types: neurobehavioral (e.g., confusion); systemic (e.g., overwhelming fatigue); gastrointestinal (e.g., bloating); and upper respiratory symptoms (e.g., stuffy nose).

Bell et al. also focused on chemical intolerance to evaluate MCS/IEI, because they suggested that chemical intolerance is one of the most specific symptoms of MCS/IEI rather than fibromyalgia or chronic fatigue syndrome. In an effort to isolate effects from disability, litigation, and expectation/attribution, Bell et al. (14–19) initiated a series of studies focused on chemical intolerance in high-functioning older and young adults from the community who were not clinically ill. Findings in these preclinical chemical intolerant individuals, who constituted 15–30% of the general population samples, included life histories of medical problems that overlapped with those of MCS/IEI patients (10, 17, 19), increased trait shyness (14, 15, 17), objectively lower total sleep times (20), evaluation of plasma beta-endorphins (21), alterations in spectral electroencephalographic patterns during chemical exposure (22) and reduced reaction times on divided-attention tasks (23).

Pathophysiological theories of MCS/IEI

There are few peer-reviewed studies that have demonstrated sufficiently strong objective correlates of reported symptoms, nor are there any studies demonstrating a new mechanism for symptom causation from chemical exposure despite some creative speculation about exposure routes in the body, sensitive tissue, and amplification processes (17, 24–29). As a result, causal hypotheses for MCS/IEI range widely between physiological and psychological mechanisms (30–34), psychosocial (35–44), belief systems (45), and enzyme, immune abnormality (46–48).

For simplification, these mechanisms may be grouped into six categories: (a) toxicologic, (b) psychophysiologic, (c) psychiatric, (d) belief systems, (e) and immune abnormality.

Toxicologic theories, or time-dependent sensitization (TDS)

Some studies suggested that theories of toxicity or organ damage attributable to immunologic or other dysfunctions remain unsupported (49, 50). In the neural-sensitization model, the following have been proposed: (1) in chemical intolerant individuals, olfactory-limbic pathways induce abnormalities in a wide range of affective, cognitive, and somatic processes via their regulatory role in the CNS (hypothalamus, amygdala, and limbic system), endocrine, and autonomic functions (33); and (2) the individual difference variable leading to amplified reactivity to low levels of chemicals is the neuropharmacological process of time-dependent sensitization (TDS) (16, 18, 51, 52). TDS is the progressive increase in a given measure with the passage of time between the initial and subsequent exposure (29, 53). Diverse pharmacological and nonpharmacological (psychological or physical stress) stimuli can initiate and elicit TDS responses, which can occur in behavioral, neurochemical, immune, and/or autonomic measures at the level of cells, organs, and/or organisms (29). Sensitizable and nonsensitizable individuals may not differ from one another at baseline or during an initial exposure, but they will differ after repeated, intermittent re-exposure (54). Exogenous stimuli must have sufficiently novel, stressful, or foreign characteristics to be capable of inducing TDS (29). However, endogenous stimuli detected in local tissue may also induce TDS in the central nervous system pathway that processes afferent information (e.g., irritable bowel syndrome (55), a diagnosis commonly reported by chemical intolerant individuals and MCS/IEI patients (10)). Notably, the results of animal studies show that the female gender (56), hyperactivity to novel substances (54), certain genetic vulnerabilities (53, 57), and/or ingestion of increased amounts of sucrose (58) are individual differences that predict heightened susceptibility to TDS. As for the olfactory system, there is evidence that sensitivity via the olfactory system is related to hypothalamic-pituitary-adrenal axis functioning, with a change of sensitivity occurring in patients with Cushing’s syndrome or with Addison’s disease by means of changing the concentration of the serum corticosteroid level (59, 60).

Otherwise, findings of neurotoxic patterns on cerebral metabolism after chemical exposure (61) lead credence to the organic origin of the neurocognitive complaints of poor memory and concentration frequently reported by MCS/IEI patients.

With regard to another pathologic explanation, Meggs (62) has posited neurogenic inflammation as a hypothesis to explain ways in which inflammation leads to further irritation upon chronic low-level exposure of volatile organic compounds, contributing to chronic rhinitis. Further, in line with neurogenic inflammation, neurogenic “switching” has been suggested as the mechanism by which the sites of inflammation are rerouted via the central nervous system to various end-organs in an attempt to explain the polysymptomatic complaints in various organ systems reported by persons with chemical intolerance.

Psychophysiologic and psychiatric theories

Some studies have proposed and have begun to demonstrate that a behaviorally conditioned response to odor could explain some MCS/IEI cases (40, 63, 64). Such severe chemical exposure may act as an unconditioned response, producing one trial learning of a conditioned psychologic response. For example, exposure to