บทฟื้นฟูวิชาการ

Multiple chemical sensitivities

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Multiple Chemical Sensitivities (MCS) is an acquired disorder characterized by recurrent, multiple-system symptoms responding to demonstrate exposure to many chemically unrelated compounds at doses far below those established in the general population to cause harmful effects. It is the most puzzling chemical syndrome and is known by many terms. The available data demonstrate that MCS patients are very heterogeneous, and that more than one causal mechanism may be responsible in different cases. It is important for diagnosis of MCS to have complete evaluation of medical histories, physical examination, and laboratory investigation. The complexity of MCS requires a comprehensive and multidisciplinary approach. Although an understanding of MCS is not clear, measures to control exposures in the workplace should be strictly done to reduce exposure to the patient as much as possible. Finally, public education about MCS is important to provide a good understanding about the illness and to prevent panic to the public.

Key words : *Chemical sensitivities, Multiple chemical sensitivities, Multiple chemical exposure, Ecological illness, Environmental illness.*

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โรคภูมิแพ้จากกลุ่มสารเคมี คือ กลุ่มโรคที่เป็น ๆ หาย ๆ เกิดกับหลายระบบอวัยวะโดยเกิดจากการสัมผัสถูกสารเคมีหลายชนิดในระดับที่ต่ำกว่าระดับที่ก่อให้เกิดพิษในคนทั่วไป โรคนี้มีชื่อหลายชื่อและเป็นโรคที่มีข้อสงสัยมากที่สุดโรคหนึ่ง ผู้ป่วยด้วยโรคนี้จะมีลักษณะที่ค่อนข้างหลากหลาย และมีความเชื่อว่าน่าจะเกิดจากกลไกหลายอย่างร่วมกัน ในการวินิจฉัยโรคนี้จำเป็นต้องซักประวัติ ตรวจร่างกาย และตรวจทางห้องปฏิบัติการอย่างละเอียดสำหรับการดูแลรักษาจะต้องให้การรักษาอย่างผสมผสานจากหลาย ๆ ด้านประกอบกัน ถึงแม้ว่าโรคนี้จะยังไม่มีข้อสรุปที่ชัดเจน แต่การควบคุมระดับสารเคมีในสถานที่ทำงานและการให้ความรู้ทั่วไปแก่ประชาชนยังคงมีความสำคัญที่จะต้องกระทำอยู่

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The term Multiple Chemical Sensitivities (MCS) was introduced by Theron Randolph in 1962 to explain a syndrome caused by exposure to foods and chemicals.[1,2] MCS is the most puzzling chemical syndrome; it is known by many terms such as environmental illness, 20th-century disease, total allergy syndrome, chemical sensitivity, ecological illness, environmental hypersensitivity or hypersusceptibility, chemical hypersensitivity syndrome, allergic toxemia, cacosmia, cerebral allergy, chemical-induced immune dysfunction, environmental irritant syndrome, environmental induced illness, gulf-war syndrome, immune system dysregulation, multiple chemical hypersensitivity syndrome, sick building syndrome, total carpet syndrome, toxic encephalopathy, and toxic response syndrome.[1,3-6]

Cullen[7] defined MCS as "an acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to demonstrable exposure to many 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 the symptoms." He also proposed the following as the major diagnostic features :[7]

1. The disorder is acquired in relation to some documentable environmental exposure(s), insult(s) or illness(es),

2. Symptoms involve more than one organ system,

3. Symptoms recur and abate in response to predictable stimuli,

4. Symptoms are elicited by exposures to chemicals of diverse structural classes and toxicological modes of action,

5. Symptoms are elicited by exposures that are demonstrable (albeit of low level),

6. Exposures that elicit symptoms must be very low (several standard deviation below levels known to cause adverse human responses), and

7. No single widely available test of organ system function can explain the symptoms.

An ad hoc committee of the Ontario Ministry of Health defined MCS in 1985 as a chronic, multisystem disorder in which patients are frequently intolerant to some chemicals and to environmental agents at usually tolerated levels, and are usually free from objective findings.[5,8-9]

Kurt[1] proposed the following characteristics of MCS:

1. Odor-triggered or exposure perceived

2. Brought on by exposures levels to chemicals below those levels considered irritating or hazardous by the United States Occupational Safety and Health Administration (OSHA) and below allergic sensitivity levels set by allergists and immunologists

3. Manifest as a multitude of neurobehavioral symptoms analogous to the panic/anxiety symptoms listed in the Diagnostic and Statistical Methods-IV-R (DSM-IV-R)

4. Lacking objective clinico-pathologic criteria beyond the vascular and autonomic changes of stress responses

5. Responsive to appropriate panic disorder management

The common features of the MCS definition were discussed in an Association of Occupational and Environmental Clinics Workshops on MCS in 1991 and are:[9]

1. Sensitivity to more than one class of chemicals

2. Symptoms involving more than one organ system

3. Symptoms occurring at exposure levels far below those affecting most people

4. Absence of any generally accepted explanation

A group of physicians referred to as clinical ecologists uses the term environmental illness to describe an acquired disease characterized by polysymptoms and multisystem disorder caused and/or exacerbated by the stress of today's exogenous influences. These exogenous influences include industrial and domestic chemicals, cigarette smoke, diesel fumes, alcoholic beverages, perfumes, food, microorganisms, in particular Candida albicans, and electromagnetic fields.[10-13]

Epidemiology

Although there is a significant number of MCS patients, there are no hard data on MCS prevalence estimates.[9,14] Mooser[3] estimated prevalence of MCS as high as 2 to 10% in the general population. The US Environmental Protection Agency (EPA)'s survey demonstrated that they were especially sensitive to one or more common chemical exposures.[15] A general population study in Baltimore showed that from 643 subjects, 66% reported symptoms to at least one of the five common chemicals surveyed.[15] A survey of the general population by random digit dial telephone survey found that from 1,027 respondents, 33% had daily or almost daily symptoms.[15]

Rea's study of 100 consecutive patients admitted to the environmental control unit at Northeast Community Hospital in Bedford, Texas found that:[3,9]

- Most (77%) were female.
- Median age was 40 years.
- Race was not indicated.
- 53.8% were highly educated, with four or more years of college.
- Most (56.3%) had symptoms before they were 30 years old.
- 58% were unable to identify a specific triggering.
- 12% associated with occupational exposures.
- 11% associated with new environment (home, job, college).
- 42.9% reported exposure to chemicals on their job as being responsible for their illnesses.

Causal Mechanism

Causal mechanism is one of the most controversial issues for MCS. The available data demonstrates that MCS patients are very heterogeneous, and that more than one causal mechanism may be responsible in different cases.[8] There are many theories to explain possible mechanisms of MCS, but no definite mechanism is accepted by the medical community. The following are the possible mechanisms:

1. **Toxicological mechanism**[2,8,13] Toxicological mechanism is one of theories for causal mechanism of MCS in which it can occur by exposure to environmental chemicals, but according to present knowledge the MCS cannot be explained by the principle of toxicology because:

(1) There is no particular symptomatology for a given chemical.

(2) Symptoms can be reacted by chemically unrelated foods and chemicals.

(3) There are no objective measurable results.

(4) There are no reproducible effects for chemical exposure in generally tolerably doses.

(5) Data on the long-term, low-level exposure effects are relatively rare.

2. Immunological mechanism[2,8,13] Various immunologic mechanisms for MCS have been proposed from case reports and clinical laboratory test data; however, the studies on the immunological status of MCS patients found that there is no evidence for alteration or impairment of their immune system. The laboratory tests which are used to demonstrate abnormal immunological status in MCS are inadequate or have widely variable reference ranges; and several tests do not have accepted and standardized laboratory protocol. There have been no controlled and blinded challenge studies showing a consistent correlation of alteration in immune findings with either specific chemical exposures or disease due to such exposure.

3. Neurophysiological mechanism Bell et al[8] proposed that subconvulsive chemical kindling of the olfactory bulb, amygdala, piriform cortex, and hippocampus, and time-dependent sensitization could intensify reactivity and reduce the response threshold to low levels of chemicals. Schusterman and Dager[8] proposed that autonomic arousal can be produced by odor and may be intensified in a person with predisposing cognitive, personality, or biologic susceptibility. However, there are no experimental data in humans to support this neurophysiological mechanism.

4. Psychological mechanism Many authors proposed that MCS resembled many psychological illnesses such as anxiety, somatization disorder, depression disorder, psychosomatic illness, and post-traumatic stress disorder.[5,7-8,15-17] Selner[2] suggested that the worst-case dimensions of MCS are often suffered by adult sequellae of physical and sexual abuse originating in early childhood. Simon et al[5] found that:

(1) Psychological factors strongly influence the development of MCS after occupational exposure to chemicals.

(2) Development of MCS is related more to an underlying trait of symptom amplification and prior psychological distress than to current psychiatric symptoms or diagnoses.

(3) A higher lifetime burden of psychiatric illness in patients who develop MCS agrees with previous findings in fibromyalgia, chronic fatigue syndrome, and chronic pelvic pain.

(4) The development of medically unexplained physical symptoms is related to previous history of anxiety or depressive disorder and to overall level of psychological distress.

(5) Chronically high levels of nonspecific dysphoric affect contribute to development and reporting of physical symptoms.

However, most of data about the above psychological mechanisms are based on case reports.

5. Conditioning mechanism[8-9,13] Another theory for mechanism of MCS is classical conditioning (Pavlovian) model. At first, an odor is associated with a strong smelling, chemical irritant exposure that causes a direct and unconditioned physical or psychophysiological response. After one or more

unconditioned stimulus, the patient becomes conditioned, and the same odor at a lower concentration can cause a conditioned response of the same symptoms.

6. **Respiratory inflammation mechanism**[8] Some authors proposed that inflammation of respiratory mucosa which amplifies the nonspecific immune response to low-level irritants is related to MCS, but it does not appear to respond to all the multiorgan system complaints in MCS patients.

7. **MCS as misdiagnosed illnesses**[8] There is an explanation that primary or misdiagnosed psychiatric disease may be the actual cause of MCS which has been based largely on clinical experience lacking standardized case definitions, examiner blinding, and appropriate comparison groups.

8. **MCS as illness belief system**[8] Some authors have postulated that in many ways MCS is a belief system promoted by clinical ecologists and those sympathetic to their views, and followed by medically unsophisticated laypersons, and that the belief is reinforced by referring patients to a network of similarly minded clinicians, and establishing support groups, hotlines, journals, and clinics to support and reinforce these beliefs.

9. **Mechanisms proposed by clinical ecologists**[1,2,6,8,10,14,16,18] Clinical ecologists are a group of physicians who claim that they are specialized in management of environmental illness. They believe that alteration in the immune system causes MCS. All of these various immunologic theories are based on a concept of "total environmental load" which suggest that the human immune system is the same as a barrel which has limited capacity to hold stresses from chemicals, food, antigens, psychosocial and infectious stressors. MCS occurs when exposures overwhelm this capacity. Chemical ecologists also proposed that Candida albicans infection is one cause of immune dysregulation.

The concepts of the clinical ecologists is not accepted by most of the medical community. The American Medical Association's Council on Scientific Affairs concluded in 1992 that MCS should not be considered a recognized clinical syndrome and there were no well-controlled studies establishing a cause of MCS. The American College of Physicians stated in 1989 that there was inadequate evidence for the concept of clinical ecology. The American Academy of Allergy and Immunology found in 1986 that there was no evidence to support the immune system dysregulation in MCS. The California Medical Association's Scientific Task Force on Clinical Ecology reported in 1986 that there was no evidence that diagnostic and treatment methods of clinical ecologists were effective. The Subcommittee on of the National Research Council also stated that there was no scientific data to support clinical diagnosis and objective treatment in MCS.[1]

Diagnosis

MCS patients are mostly middle aged, well-educated women who are interested in their diagnosis, attend support groups, read the literature, develop friendships with the same patients, have a dissatisfaction with traditional medical treatment, reject the psychological, physician, and somatic

etiology, and frequent change of doctors.[13,16]

History of illness Symptoms usually start after a single heavy exposure to a substance, with recurrent exposure to low levels of the same substance such as odor or fragrances.[1] Symptoms were usually subjective; although the symptoms of affected individuals vary, they are commonly related to the multiorgan system and the predominant central nervous system symptoms.[4,11] Symptoms consist of headaches, fatigue, loss of concentration, mental status changes, visual abnormalities, peripheral neuropathies, cardiac conduction system anomalies, respiratory symptoms, and other nonspecific symptoms.[1,4,10-13]

It is important for diagnosis of MCS to have complete evaluation of the medical histories, past medical and psychiatric histories, and industrial hygiene data regarding the patient's exposures; psychiatric evaluation may be appropriate for some patients.[4,14,19]

Physical examination A comprehensive medical and psychosocial evaluation of the patient should be performed.[19] Neuropsychological testing may be useful to rule out other conditions in the differential diagnosis.[19] Physical examination is usually normal in MCS patients.[4,18]

Laboratory examination Diagnostic testing in MCS patients is necessary to rule out other environmental or nonenvironmental illness or treatable disease conditions in the differential diagnosis. Also, a trial removal from the environmental chemical exposure for a short time may be useful in some cases. It is usually found that laboratory tests in MCS patients are normal or change slightly without significance.[19]

Clinical ecology diagnosis Clinical ecology diagnosis of MCS is based on the provocation-neutralization technique, in which the patient records symptoms after being applied with a test dose of a chemical, food extract, or allergen as a sublingual drop, by subcutaneous or intracutaneous injection.[6,18] However, there is no evidence of symptom provocation by subneutralizing concentration.[19] Staudenmayer et al[9] found that during 145 double-blind provocation chamber challenges of 20 MCS patients, sensitivity was 33%, specificity 65%,and efficiency 52%, or no better than chance alone.

Treatment

The complexity of MCS requires a comprehensive and multidisciplinary approach.[14,20] A multidisciplinary approach should be directed to the chronic aspects of the patients and should involve other professionals such as psychologists, social workers, physical therapists, occupational therapists, psychological counselors, vocational rehabilitation counselors, and others.[20] The doctor-patient relationship also serves as an important tool in the treatment of MCS.[14] The physician should understand the patient's interactions with his or her social environment, and should provide support in the patient's relationships with family, employer, coworkers, legal advocates, other health providers and insurance carriers.[20-21] The aim of the clinical management programs is to control the symptom and improve functional ability rather than a cure of the disease.[19] Pharmacological treatment may be used to relieve the psychophysiological symptoms that relate to chemical sensitivity.[19] If the patient's illness was caused by chemical exposure in the workplace, it is necessary

to remove the patient from the exposure and provide engineering controls, personal protective equipment, work practice, and job modification.[19-20] Patient education is important to provide under-standing of the role of stress on his or her illness, and to enhance the patient's sense of control over the workplace or home stressors including the environmental chemical exposures on daily life; education includes general principles of toxicology, industrial hygiene measures available to reduce exposures, host factors and others.[19-20] The treatment of coexisting psychiatric manifestations is likely to reduce symptoms and disability.[19] Specific cognitive and behavioral interventions in achieving symptomatic desensitization may also be useful in the treatment of some patients; the principle of behavioral interventions is symptom desensitization by gradually exposing the patients to substances or situations associated with symptoms and allow them to accommodate and increase tolerance by an organized program.[17,19]

Clinical ecology treatment consists basically of avoidance of identified or suspected excitant exposures such as perfumes, cosmetics, deodorants, synthetic clothing, soft plastics, carpet and solvents; most patients are prescribed neutralization treatment by subcutaneous and/or sublingual administration of antigen which is indicated by the excitants.[6,10,12-13,18] Additionally, treatments include using a rotary diversified diet of compatible food and water that is chemically less contaminated, antioxidants, megadoses of vitamins, antimycotic drugs, enemas, sweating cures, and specific antigen immuno-therapy.[10,12-13,18] Terr[18] studied 50 cases treated by clinical ecologists and found that all 50 patients were advised to avoid chemicals and other exposure, 28% were advised to move from their urban homes to a rural area, 74% were advised to eat a rotatory diversified diet, 62% were given neutralizing antigens, but drug therapy was not recommended.[24] He also found that only two of 50 cases had evidence of improvement. Other authors recommended that the role of complete avoidance of chemical exposures does not help to improve the patient's illness; in contrast, avoidance can lead to severe social isolation when the patients avoid contact with offending chemicals found in friends' or relatives' houses, clothing, or perfume.[15-16,19,21] These treatments are also expensive; for example, one subject spent more than $40,000 to rebuild a new home according to environmental illness standards.[16]

Research needed

The most immediate need is to expand descriptive studies characterizing the clinical and demographic features of MCS and to elucidate the natural history, general patterns of response to social and chemical interventions; also, there is a need for and analytic studies to elucidate factors which are associated with MCS and which might be causal.[22] Research is needed to determine actual prevalence and incidence of MCS in various populations.[8]

Further clarification of etiologic mechanisms in MCS is also necessary; for example, controlled and objective measurement of the possible neurophysiological effects of odor or respiratory tract irritation from low levels of chemicals.[8] Further research is needed to develop strategies, new and more effective approaches, and prevention.[19]

Controlled clinical trials of diagnostic and treatment methods would be done under scientific

methods.[8,22] Definitive research on controlled challenge procedures is necessary before being used for diagnosis.[19] Controlled clinical research in the various psychiatric, behavioral, and other treatments in different categories of MCS patients is needed.[8] Development of an animal model of MCS by one or more interventions which is similar to human experience should be done.[22]

Conclusion

In the practical point of view, it is difficult to diagnose and manage MCS patients. In the present day, there is no consensus about MCS yet. There are 2 major opposite opinions about MCS as mentioned above. Therefore, we should be careful before we diagnose someone as MCS and we should give an appropriate treatment to them. Also, as more chemicals have been used in the workplace and in the environment around us, we should be aware of MCS as one of the diseases in the industrial era.

MCS is the most problematic environmental disease at the present. Understanding the mechanism of MCS can help to develop strategies for diagnosis, treatment, and prevention. Although the understanding of MCS is not clear, measures to control exposures in the workplace should be strictly done to reduce exposure to the patient as much as possible. Scientific methods should be included in diagnostic and treatment methods. Finally, public education about MCS is important to provide a good understanding about the illness, and to prevent panic to the public.

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