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CHILDREN'S HOSPITAL BOSTON HARVARD MEDICAL SCHOOL

# A 4-Year-Old Girl with Manifestations of Multiple Chemical Sensitivities

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Multiple chemical sensitivities (MCS) syndrome, also known as idiopathic environmental intolerance, is a controversial diagnosis that encompasses a wide range of waxing and waning, subjective symptoms referable to more than one body system and provoked by exposure to low levels of chemicals, foods, or other agents in the environment. Although MCS has been studied extensively, a unifying mechanism explaining the illness remains obscure, and clinicians are divided as to whether such a medical entity exists separately from psychosomatic syndromes. MCS is an adult diagnosis; there is little reference to pediatric cases in the scientific literature. In this case from the Pediatric Environmental Health Subspecialty Unit at Boston's Children's Hospital, I present the case of a preschool child who had suffered from milk allergy and poor weight gain as an infant, and then later developed asthma, allergic symptoms, sinusitis, headaches, fatigue, and rashes precipitated by an expanding variety of chemicals, foods, and allergens. I review definitions, mechanisms, diagnostic strategies, and management, and discuss some uniquely pediatric features of MCS as illustrated by this case. *Key words* idiopathic environmental intolerance, multiple chemical sensitivities. *Environ Health Perspect* 108:1219–1223 (2000). [Online 20 November 2000] *http://ehpnet1.niehs.nih.gov/docs/2000/108p1219-1223woolf/abstract.html* 

#### Case

A young girl (4 years 11 months of age) was referred to the Pediatric Environmental Health Subspecialty Unit at Boston's Children's Hospital (PEHSU) for evaluation. She had been previously diagnosed by her pediatrician as having allergies, frequent otitis media, congestion, sinusitis, and reactive airway disease, with cough-equivalent bronchospasm especially prominent during upper respiratory infections and exercise. During infancy the patient had been diagnosed with poor weight gain due to a milk allergy and treated with an elemental milk and then soy formula. There was a family history of atopy; the father and secondary relatives had childhood asthma and hay fever. Previous allergy testing was positive only for cat dander; therapy included inhaled bronchodilators, steroids, antihistamines, and cromolyn.

At home, the family allowed no tobacco smoking and had reordered the house to make it more habitable for the patient. They had removed all carpeting and covered the mattress on the child's bed. The house was frequently dusted and the gas-fired furnace and ductwork were regularly cleaned.

The patient's mother was concerned that her daughter's symptoms were becoming worse with a variety of environmental triggers and an expanding list of symptoms. Volatile organic chemicals, cleaning compounds, detergents, perfumes, cigarette smoke, dust, and paints caused new symptoms of pruritis, headache, fatigue, nausea, difficulty breathing, and malaise. The patient was on a restricted and rotating diet, which included goat cheese and duck eggs, because of her food allergies to citrus, seafood, foods containing preservatives, and meats. The parents had purchased only all-cotton clothing for the patient because polyesters and other artificial fibers made her itch and reportedly caused rashes. The parents had also sought help from a naturopath, who had found multiple allergies. The patient was regularly given certain herbal preparations, including echinacea, astralagus, pulsatilla, bryonia, forscolin, and quercidin, with some relief of symptoms, according to the parents.

The child frequently had olfactory warning when chemicals in the environment were going to exacerbate her symptoms; whenever she voiced her anxieties, the family then quickly left the environment. Thus the patient had begun to severely limit her activities because of her multiple chemical sensitivities (MCS). For example, the mother no longer took her daughter into public restrooms or grocery stores because the disinfectants caused dizziness, fatigue, headache, chest tightness, and nausea. After the patient visited the PEHSU, her mother complained that some areas of the hospital had been freshly painted and that the patient had later become symptomatic with an asthma attack. She feared that the patient's imminent transition into public school kindergarten would likely be sabotaged by the school's routine use of pesticides and cleaning products. The school had supplied her in advance with material safety data sheets covering 15 commercial products, which contained more than 35 chemicals applied indoors during the routine maintenance at the school. School officials denied that any renovations were planned, but they promised to work with the parents to limit the patient's contact with chemical exposures.

A physical examination revealed a frailappearing child with no evidence of rashes or eczema. The eye, nose, and throat exam showed mild nasal turbinate swelling and redness, but no involvement of the conjunctiva or throat. The patient's lungs were clear, and the heart and abdomen, as well as the rest of the exam, were within normal limits. Previous blood work, including peripheral eosinophil count and serum IgE level, was negative or normal.

The family was counseled about keeping a home symptom diary. Pulmonary function testing was recommended when the patient becomes old enough to cooperate. Coping measures and feedback to empower the patient were discussed. Anticipatory guidance was given on working with school officials to limit the environmental impact on the patient's school attendance. Follow-up 9 months later revealed continued respiratory and other symptoms with limited effectiveness of avoidance strategies, environmental controls, herbs, and medications. The patient had missed 15 days of her half-day kindergarten due to her symptoms, which seemed to be worsened by the school's use of a new carpet-cleaning solution.

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A controversial syndrome in adults known as MCS is characterized by a range of disparate symptoms involving the skin, vascular, genitourinary, musculoskeletal, gastrointestinal, pulmonary, and central nervous systems, which are "triggered" by low-dose exposures to chemicals, foods, biologicals, or other toxic agents in the environment. Often adult MCS syndrome is initially precipitated by an exposure to a chemical in the workplace; subsequently the patient develops more and more intolerance to an array of foods, chemicals, and other "incitants" until he or she is functionally disabled. However, many clinicians question the validity of MCS as a medical entity and include it among "fashionable diagnoses" such as chronic fatigue syndrome or fibromyalgia, representing somatization of essentially psychologic complaints (1). Clinicians, researchers, and health policy makers cannot even agree on the name of this entity. MCS is also known as idiopathic environmental intolerance, environmental illness, environmental hypersensitivity, and universal reactors. MCS as a construct is felt by some to overlap with sick building syndrome (2,3) or the Gulf War syndrome (4,5).

MCS was recently reviewed by Kipen and Fiedler ( $\delta$ ). Yet children, such as the case presented here, whose illnesses resemble the adult syndrome of MCS have been referred to our PEHSU. The American Academy of Pediatrics includes MCS in its recently published *Handbook of Pediatric Environmental Health*, but offers no diagnostic criteria ( $\partial$ ). Indeed it suggests that such diverse childhood maladies as attention deficits, learning disorders, sick building syndrome, and hyperactivity syndromes can share elements with and overlap MCS.

**Pediatric case definition.** The case described in this paper meets certain definitional characterstics of MCS, such as a) effects on more than one body system; b) the occurrence of a variety of chemical, food, and biologic agent triggers at low-level concentrations; c) spreading of the incitant agents responsible for symptoms; d) progressive involvement of body systems; and *e*) the lack of a diagnostic or an abnormal laboratory assay. Although this child had been previously diagnosed with milk intolerance, asthma, and sinusitis, no one unifying set of diagnoses or explanations seemed to satisfy her range of symptoms or the progressive nature of her sensitivities. As the case with this child, many adults with MCS report the spreading nature of their intolerance to lowlevel environmental toxic agents-more and more toxicants must be avoided as time goes on. Diverse precipitants of symptoms have been postulated: biological agents, electromagnetic radiation, off-gassing construction

materials and home decorations, foods, pesticides, synthetics, perfumes, other toiletries, and the like are cited as common offenders.

The diagnosis of MCS in children differs from that in adults in some significant ways. For example, many adults with MCS cite a workplace chemical exposure as the precipitant of the disease, and the illness has been addressed as an occupational health issue (8-12). For children, the incitant is more likely to be found in the home or school. Many symptoms in adults are subjective and often include fatigue, malaise, headache, dizziness, burning sensations, breathlessness, a "mental fog" of impaired cognition, and paresthesias; no objective laboratory abnormalities characterize the disorder. In the case presented here, the parents largely provided the history (and the interpretation) of the child's symptoms, complaints, and reactions. Young children are often not able to pinpoint or articulate their own symptoms well. They cannot recall the time course of their own symptoms or associated findings, and clinicians must rely on parents to recount their observations of their child's health. Because there is no single objective test finding to confirm the diagnosis of MCS, its diagnosis in children will often rest largely on historical information obtained from the parents.

MCS definitional criteria have been previously devised for adults (13); these are summarized in Table 1, but modified to be more applicable to pediatric cases. The progressive nature of symptoms titered to smaller and smaller doses of precipitants (triggers, allergens, incitants), the olfactory warning of offending odors, and the progressive restrictions upon the patient's activities and habitable environments all characterize the unfortunate victims of this condition, although there is no unifying theme that covers the spectrum of MCS syndrome.

*Etiologic theories.* The etiology of MCS syndrome remains a mystery. Mechanisms postulated to explain MCS have been reviewed in detail elsewhere (6, 14, 15). Although immune disorders have been invoked, there are no convincing scientific studies that document any specific immune abnormalities in patients with MCS (16, 17). Olfactory warning of noxious odors seems to be a hallmark of MCS; a mechanism of neurotoxicity from chemical toxicants carried to the central nervous system (hypothalamus, amygdala, and limbic system) by way of the olfactory bulb has been offered as one mechanism of causation (18-20). Similar sensitization of the nervous system via the respiratory tract (instead of the olfactory bulb) by the inhalation of low-dose toxicants has been postulated (21), but in an attempt to measure pulmonary function changes during provocative challenges to 15 patients with MCS, Leznoff (22) could not document any abnormalities. Learned behaviors conditioned by olfactory sensitization or "limbic kindling" as a phobic response to chemical "triggers" have been discounted by Staudenmayer (23) as unproven, without any physiologic basis, and no different from simple panic attacks. None of these theories has been validated by scientific, methodologically sound research and none has been investigated in pediatric patients.

**Pediatric diagnosis.** The diagnostic criteria outlined in Table 1 seem generalizable to children, and could tentatively be used as a guide for clinicians evaluating pediatric cases, although such definitional issues have not been scientifically explored in children. The diagnosis of MCS in children involves a careful medical and environmental history and a

Table 1. Clinical diagnostic criteria of MCS syndrome in children.

- Responses to offending environmental toxicants occur at levels of exposure below the 2.5 percentile for response in the general population Child responds to multiple substances that are unrelated chemically (i.e., causes lack specificity). The symptoms are not confined to one or several environments (e.g., only sick buildings) Biologic plausibility, identifiable exposure Symptoms are reproducible with exposure with reasonable consistency Symptoms resolve after removal of incitant exposures An identifiable exposure preceded the onset of the problem
- Topology of responses
- Adverse responses affect more than one bodily system
- Primary complaints include neuro-psychologic symptoms
- The child exhibits altered sensitivity to odor
- Persisting nature of perceived changes
- The disorder is chronic
- Differential diagnosis
- No single, accepted test of physiologic function correlates with the symptoms
- Subjective responses and ameliorative actions of affected children
- The caretakers and/or child perceive the child's response as unpleasant or disturbing
- The family has sought professional advice
- The individual's caretakers believe he or she has a disorder

The family takes action to avoid exposures to symptom-inducing chemicals

Nature of incitants provoking a response

Modified from Nethercott et al. (13).

detailed physical examination. Testing of hair, blood, urine, or other tissues as a screening measure for excessive environmental toxins is generally not helpful. The assessment should be directed toward the exclusion of other diagnoses, such as asthma, simple migraine, allergies, or an immune disorder. Radioallergosorbent tests, serum IgE concentrations, and skin testing for common allergens may be helpful diagnostic procedures in some children to confirm a diagnosis of atopy or allergies. Pulmonary function testing may reveal airway obstruction in cases of childhood asthma.

Alternative practitioners who call themselves "environmental practitioners" or "clinical ecologists" claim that provocation-neutralization challenges by sublingual or dermal application or parenteral injection of the identified toxicants can diagnose adults with MCS. However, the American College of Physicians reviewed 15 studies of provocation-neutralization testing performed by clinical ecologists and criticized the introduction of bias, lack of controls, and their uniformly poor methodologic designs (24). There is little information about whether such diagnostic tests have been applied to children or have any use in the diagnosis of childhood MCS.

**Psychiatric conditions.** Previous studies in adults have suggested a strong psychologic component to MCS. Some victims of MCS were found to have attention-seeking, borderline personalities, panic attacks, other anxiety or affective disorders, or other somatoform syndromes (23,25–28). Such findings suggest that children presenting with symptoms resembling MCS should be assessed for psychiatric complaints, although there are no pediatric studies of psychologic comorbidities in MCS.

Family dynamics and MCS. The evaluation of MCS in children should include a careful family history of psychiatric and medical conditions. A positive family history for psychiatric diagnoses and treatment may be common in victims of MCS (29). Comorbidities such as posttraumatic stress syndrome or childhood physical or sexual abuse may also have roles as underlying determinants of vulnerability to the later development of MCS in adulthood (23). There are no pediatric reports in which MCS was found to be the presenting manifestation of underlying child physical or sexual abuse; however, the parent-child relationship must be examined. A careful assessment of the parents' level of anxiety, their interpretations of home or school-related events, and their reactions to the clinician's proffered advice is important in the evaluation of the child. If a form of abuse is suspected, consultation with social services

and/or a trial of separation of the child from the parent may be warranted.

Parental preconceptions and expectations can shape their interactions with and beliefs about their children's health, reinforcing or extinguishing a child's behaviors or erroneously attributing their symptoms to environmental precipitants. For many (but not all) such families, MCS may serve as a coping strategy or a more socially acceptable medical condition within which to express depressive symptomatology. Children may be attracted to the attention they gain when they are in the dependency role of patient. Sometimes such belief systems may become fixed because of a high level of parental anxiety about the child's health and their perception of the child's vulnerability to harmful toxins. In certain circumstances, diagnoses such as school phobia, psychiatric disorders of the parents and/or children, or other dysfunctional family dynamics must be considered with the differential diagnosis in the evaluation of children presenting ostensibly with MCS syndrome.

Factitious histories may complicate the diagnosis of MCS. Munchausen by proxy syndrome (MbPS) has been defined as fabricated history (30,31) in which a) a child's medical problems do not respond to treatment or they follow an unusual course; b) physical and laboratory findings made in relation to the illness cannot be explained, are very unusual, or are considered implausible; c) the signs and symptoms of a child's illness fail to occur in the parent's absence; d) the family history discloses numerous medical problems that are difficult to substantiate, and their veracity is doubtful; and e) the family history discloses similar unexplained illness in other children.

Meadow (32) warned clinicians not to confuse MbPS with such problems as unrecognized physical abuse, failure to thrive, overanxious parents, parents with a delusional disorder, school phobia, "hysteria by proxy," or simple "doctor shopping." These alternative diagnoses should be considered in childhood cases of MCS syndrome as well. Some cases of childhood MCS may overlap with MbPS, based on the above definition. In a case series of men as perpetrators of MbPS, Meadow (33) described one father who was treating his 4-year-old son for alleged bowel disorders, allergy, and anemia with bizarre diets and enemas. Another father claimed that there were dangerous gas and water supplies causing the illness, leading to formal complaints and litigation against the public utilities (33).

Likewise, practitioners may buy into the parent's view of the illness because "medicalization" of the condition allows for easier diagnostic and treatment options than does the investigation and management of the complaints within the context of a psychosomatic syndrome.

Diagnostic and psychosocial issues of children suffering from an MCS-like syndrome are outlined in Table 2.

*Use of health care.* The demands of adult patients with MCS on health care professionals, their high use of health care resources, and their dissatisfaction with proffered advice, especially if that advice suggests psychologic counseling as a management option, are frustrating for both parties. Adult MCS patients are high-frequency users of medical facilities and suffer a considerable amount of functional disability because of their complaints and the strategies they must employ to get through the day (35). Parental over-use of services can be frustrating to pediatric health care providers, who must nevertheless continue to offer both their availability and support in the best interests of the child.

**Environmental restrictions.** Many patients restrict their activities and reconstruct their habitats so that they can avoid the environmental agents that cause symptoms, essentially living in a relatively chemical-free environment. Some adults use barrier clothing such as special masks, gloves, coveralls, and even self-contained breathing apparatus in the attempt to avoid chemical triggers. The disability in an adult is that he or she is isolated from others socially and cannot hold a job (35). Children who cannot attend school or develop normal peer relationships because of MCS syndrome would be similarly disabled (36, 37). As illustrated by the case of this 4-year-old girl, caretakers may sometimes require that schools provide prior notification of their intended use of pesticides or other chemicals on school grounds so that children can be kept at home on those days. There are pressures on legislators to mandate that public places be chemical-free so that symptoms are not provoked in sensitive individuals (38), as mentioned in the "Public health and psychosocial issues" in Table 2.

Dietary modifications and other remedies. Therapies for MCS syndrome have included restricted diets and avoidance of environmental triggers. Patients with MCS syndrome seek out a variety of treatments not only from physicians but also clinical ecologists, naturopaths, and other practitioners. Clinical ecologists use a number of unproven therapies, such as rotating diversified diets or desensitization routines that include frequent injections or sublingual or dermal application of incitants.

Clinical ecologists and other alternative practitioners may recommend herbs and minerals to treat their patients by improving their tolerance of the environment (*39*). Some clinical ecologists postulate that MCS sufferers have deficits of essential cofactors or enzymes necessary for chemical detoxification; they prescribe dietary supplements, oxygen, antioxidants, or vitamins to repair such unproven deficiencies. Clearly allergic symptoms may respond to desensitization, bronchodilators, and other allergy medications; however, medications are rarely used as treatments by alternative practitioners.

As outlined in Table 2, some therapies used to treat MCS hold special risks for children, and their use should be discouraged. Herbal products used to treat children can be harmful as well as beneficial (40). Parents should be warned against using potentially harmful and expensive remedies, such as repeated catharsis, gamma globulin injections, chelation, or "sweat therapies," advocated by some practitioners when there is no scientific evidence that these are effective strategies for the treatment of MCS. Infants and young children are generally more susceptible than adults to cathartics (41) and to dehydration and electrolyte abnormalities by virtue of their small size, restricted access to replacement fluids, and immature renal concentrating system (42).

*Psychologic approaches and coping strategies.* Newer biopsychologic modalities of management, including biofeedback, electrophysiologic monitoring, coping strategies, family-centered therapy, and behavioral modification (psychologic desensitization) techniques, are worth investigating in children (*43*). Breaking through the mistrust of families and their hostility to allopathic medicine is important; MCS-affected children and their parents must be accorded the same compassion and respect given to all other groups of patients ( $\vec{A}$ ). School systems, social services, and other community-based agencies should offer to work with families in helping to cope with the illness.

Future studies. The Council on Scientific Affairs of the American Medical Association, the American College of Physicians, the American College of Occupational and Environmental Medicine, and other professional groups have all issued position papers that are openly skeptical of MCS as a distinct medical entity (15,24,44). They call for more scientific research into the tenets of clinical ecology and MCS in order to subject the numerous theories concerning these disorders to the peer review of evidence-based, controlled investigation. Research is made more difficult because of the lack of objective findings; some patients claim that their chemical sensitivities may shift from one chemical agent to another without warning. The olfactory warning invoked by MCS sufferers makes the design of double-blinded studies problematic. Whatever the difficulties, such scientific investigations should also be extended to children whose complaints resemble those of adults suffering from MCS syndrome so that better solutions can be offered to those children and their families disabled by this disorder.

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Diagnosis	There is no agreed upon case definition of MCS in adults and little that is evidence-based in the diagnosis or treatment of adults. There is even less known about children so diagnosed.
	It has been proposed that children's learning disorders or attentional deficit hyperactivity disorder (ADHD) might be explained by MCS, but without any convincing scientific evidence.
	Adults with MCS have often been diagnosed with psychiatric conditions such as anxiety neurosis, somatoform syndromes, or depression. It is unknown whether affected children or their parents or caretakers have specific psychiatric diagnoses. However, it seems evident that they are living with considerable psychosocial stress and pain.
Management	Parents will frequently shop for a doctor and seek alternative practitioners because of their frustrations and dissatisfaction with the response of physicians to their child's MCS.
	It may be difficult for health care providers to communicate with parents who hold such a system of fixed beliefs about their child's ill health and perceived environmental toxins.
	Therapies recommended by clinical ecologists may engender additional risks if used for children. For example, severely restricted diets can interfere with the basic nutritional requirements needed for normal growth and development.
	Other therapies recommended, such as desensitization, herbs, or vitamins, may be especially harmful to children, whose developing body systems (e.g. central nervous and immune systems) are particularly vulnerable to injury.
	Young children may have a limited capacity to detoxify certain herbs, hormones, and remedies through the liver and kidneys, with a consequent higher risk of toxic reactions.
	Infants and young children are particularly vulnerable to fluid and electrolyte imbalances provoked by laxatives or purging; they may not have the capacity to detoxify and eliminate herbs, minerals, and dietary supplements used by clinical ecologists and other practitioners as remedies in adults.
Public health and psychosocial issues	Many adult MCS patients implicate an incident in the workplace that involved a chemical exposure as the inciting agent. For children, school or home would logically be the commonly implicated site of the triggering exposure to a food, drug, or chemical. The social isolation that accompanies chemical avoidance strategies is particularly disabling for children. Such isolation impairs a child's ability to make friends and otherwise interferes with normal psychosocial development. Avoidance of school may impair their intellectual development.
	Children as well as adults are entitled to the same protections afforded by federal laws under the Americans with Disabilities Act ( <i>34</i> ). This federal law has been applied to include patients with MCS. For children, the law could be interpreted to include prior notification of parents if pesticide spraying or other chemical applications were planned at a school or day care center. The law might mandate other accommodation of the special needs of a child with MCS. Children depend on adults to make responsible choices concerning their health that are in their best interests. The diagnosis of MCS can lead to lifestyle choices that may add stress to family relationships, especially if parents disagree between themselves or with

Table 2. Pediatric considerations in multiple chemical sensitivities.

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