Review Article

Chemical Sensitivity: Pathophysiology or Pathopsychology?

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ABSTRACT

Background: Escalating numbers of people throughout the world are presenting to primary care physicians, allergists, and immunologists with myriad clinical symptoms after low-level exposure to assorted everyday chemicals such as smoke, perfumes, air fresheners, paints, glues, and other products. This clinical state is referred to by various diagnostic labels, including multiple chemical sensitivity disorder, environmental intolerance, chemical sensitivity (CS), and sensitivity-related illness, and has been the subject of much controversy within the health care community.

Objective: The goal of this study was to provide a brief overview of the etiology, pathogenesis, clinical presentation, and management of CS. An evaluation of the medical community's response to this emerging diagnosis was also explored.

Methods: This review was prepared by assessing available medical and scientific literature from MEDLINE, as well as by reviewing numerous books, toxicology journals, conference proceedings, government publications, and environmental health periodicals. A primary observation, however, is that there is limited scientific literature available on the issue of CS. The format of a traditional integrated review was chosen because such reviews play a pivotal role in scientific research and professional practice in medical issues with limited primary study and uncharted clinical territory.

Results: The sensitization state of CS seems to be initiated by a significant toxic exposure, occurring as a 1-time event, or on surpassing a threshold of toxicity after toxicant accrual from repeated lower-level exposures. Once sensitized through a toxicant-induced loss of tolerance, individuals exposed to inciting triggers such as minute amounts of diverse everyday chemicals may experience various clinical and immune sequelae, sometimes involving lymphocyte, antibody, or cytokine responses. Precautionary avoidance of inciting triggers will prevent symptoms, and desensitization immunotherapy or immune suppression may improve symptoms in some cases. Sustained resolution of the CS state occurs after successful elimination of the accrued body burden of toxicants through natural mechanisms of toxicant bioelimination and/or interventions of clinical detoxification. Despite extensive clinical evidence to support the veracity of this clinical state, many members of the medical community are reluctant to accept this condition as a pathophysiologic disorder.

Conclusions: The emerging problem of ubiquitous adverse toxicant exposures in modern society has resulted in escalating numbers of individuals developing a CS disorder. As usual in medical history, iconoclastic ideas and emerging evidence regarding novel disease mechanisms, such as the pathogenesis of CS, have been met with controversy, resistance, and sluggish knowledge translation. (*Clin Ther.* 2013;35:572–577)

Key words: chemical sensitivity, clinical detoxification, environmental intolerance, multiple chemical sensitivity disorder, sensitivity-related illness, toxicant-induced loss of tolerance.

> *Predetermined politicized positions are precisely what science supposedly repudiates.*
>
> *-Matthew Hanley*

INTRODUCTION

Food intolerance and chemical sensitivity (CS) were seemingly infrequent problems in society 50 years ago. Currently, however, an increasing proportion of the pediatric and adult population in the developed world experiences adverse reactions elicited by exposure to low concentrations of not only antigenic stimuli such as foods or inhalants but also to chemicals that are well

Accepted for publication April 11, 2013.
http://dx.doi.org/10.1016/j.clinthera.2013.04.003
0149-2918/$ - see front matter

tolerated by the majority. Furthermore, not all such sensitivity reactions represent the classically understood concept of "allergic" phenomenon involving immunoglobulin(Ig) E antibody-mediated response. The occurrence of alleged hyperreactivity to diverse everyday chemical incitants, sometimes referred to as multiple chemical sensitivity or just CS, now seems to seriously affect ~3% to 4% of the general population, including children,[1,2] and has become an increasing public health dilemma[3] in many jurisdictions throughout the globe.[2,4–6]

As is common with heretofore unexplained conditions, patients presenting with CS have been received unsympathetically by some medical practitioners.[7] Often thought to be a manifestation of disordered psychology, many researchers and clinicians have rejected CS as a pathophysiologic condition. Some have welcomed the forthcoming American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Revision*, diagnosis of somatic symptoms disorder[8] as a fitting diagnostic category for attribution of this clinical presentation. A mounting body of evidence, however, suggests that the millions of individuals suffering from this apparently new CS disorder have common features and may have a common etiology. This brief review provides an introduction to the baffling condition of CS.

RESULTS

Etiology of CS States

Over the last 50 years, our culture has experienced an unprecedented chemical revolution with the manufacture and release of myriad synthetic chemical agents into our homes, workplaces, and schools.[9] Major medical bodies such as the Centers for Disease Control and Prevention have established that many people in the population maintain a toxicant burden.[10] Considerable evidence has linked diverse health concerns to intense, acute exposure, as well as to repeated low-level exposure, to potentially toxic agents.[9] It is noteworthy that many observational studies have found that assorted types of toxicant exposure, including chemicals and biologic agents such as mold, generally precede the development of CS states.[11] Furthermore, the epidemiologic escalation of CS in the general population parallels the rising prevalence of toxicant exposures by population groups.

Individuals occupationally exposed to various adverse agents, for example, have an increased prevalence of CS,[12,13] with major differences between exposed versus nonexposed employees within the same occupation.[12] Many articles discuss the initiation of sensitivity issues after contaminated air exposure within building settings.[14–19] Following the 9/11 disaster and recent warfare such as the conflict in the Persian Gulf, many participants working in toxicant replete milieus subsequently developed CS states that were non-existent before the exposures.[20–24] Newly established CS was also documented in many survivors of the 1984 Bhopal industrial catastrophe after their exposure to various toxins released by a pesticide plant.[25] In research settings, it is possible to induce sensitivity states in animals by exposing them to toxic insults.[26–28]

It thus seems that exogenous toxic exposures initiate a hypersensitive immune state, whereby the immune response subsequently becomes dysregulated with a consequent toxicant-induced loss of tolerance[29] to minute exposures of compounds such as diverse chemicals. (**Figure**) The degree of hypersensitivity is dynamic and appears to parallel the scale of the total body burden of bioaccumulated toxicants. A clinical outcome ensues in which these minute exposures to

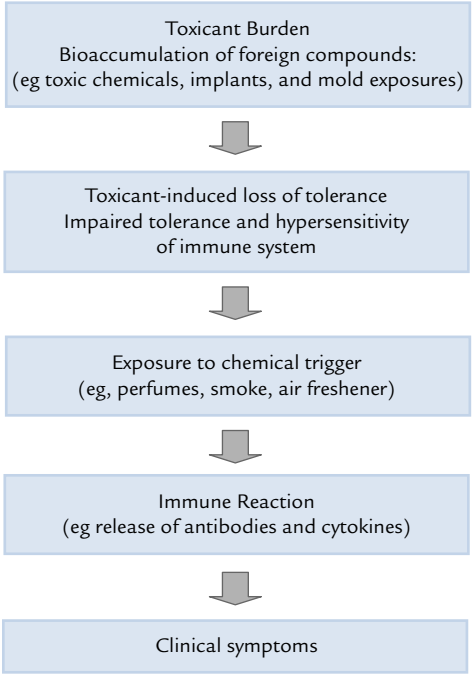

Figure. Mechanism of development of chemical sensitivity.