

# Co-Morbidity of Multiple Chemical Sensitivity (MCS) and Chronic Fatigue Syndrome (CFS): Which Comes First

Harold I. Zeliger<sup>1, \*</sup>, Bernard Possidente<sup>2</sup>, Abby G. Drake<sup>2</sup>

<sup>1</sup>Zeliger Research and Consulting, Department of Toxicology, Cape Elizabeth, Maine, USA

<sup>2</sup>Department of Biology, Skidmore College, Saratoga Springs, New York, USA

## Abstract

The co-morbidity of multiple chemical sensitivity (MCS) and chronic fatigue syndrome (CFS) has previously been reported. The present study was aimed to ascertain if either of the two conditions preceded the other in individuals affected with both conditions. An online survey of patients suffering from both MCS and CFS was undertaken. Those suffering from both of these conditions were asked which condition preceded the other. The results showed that 58% of the respondents were co-morbid with both conditions. Approximately half of the respondents reported the onset of MCS first (54%) while approximately half (46%) reported the prior onset of CFS. It is concluded that there is no significant bias with respect to either condition preceding the other in cases of co-morbidity. A mechanism for the onset of these diseases and suggestions for lowering their incidences are made.

## Keywords

Multiple Chemical Sensitivity, Chronic Fatigue Syndrome, Environmental Disease, Disease Co-Morbidity

Received: March 18, 2015 / Accepted: May 22, 2015 / Published online: June 28, 2015

© 2015 The Authors. Published by American Institute of Science. This Open Access article is under the CC BY-NC license.

<http://creativecommons.org/licenses/by-nc/4.0/>

## 1. Introduction

Multiple chemical sensitivity (MCS), also known as chemical hypersensitivity, is a chronic condition in which individuals are acutely hypersensitive to low levels of chemicals that others are not affected by. Symptoms are produced upon exposure to chemicals contained in paints, pesticides, adhesives, perfumes and other products containing volatile organic compounds. Multiple systems of the body are affected upon exposure, including the immunological, neurological and endocrine systems [1]. Symptoms generally improve or resolve when the affecting chemical agents are removed [2,3]. MCS is believed to affect between 6 and 15% of the population in the United States [2,4]. Chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME), is a chronic condition that can affect virtually every major system in the body, including the immunological,

neurological, hormonal, gastrointestinal and musculoskeletal systems [2]. Symptoms are produced upon contraction of bacterial or viral disease, exposures to chemicals, physical exertion and stress. Symptoms include persistent fatigue lasting for 6 or more consecutive months that is not due to exertion or other medical conditions associated with fatigue, fatigue that significantly interferes with daily activities and work, impaired memory, anxiety, difficulty sleeping with un-refreshing sleep and joint and muscular pain [5]. The precise number of people with CFS is unknown. Estimates of the prevalence of CFS range from 0.42 to greater than 1.0% of the population and it is estimated that nearly one million Americans are affected with CFS [2, 6, 7]. CFS is three to four times more prevalent in women than in men, but the gender ratio is almost equal in children with CFS [7]. The reason for this gender differences remains unknown. The co-morbidity of multiple chemical sensitivity and chronic fatigue syndrome has been previously reported. It is estimated that between 30

\* Corresponding author

E-mail address: [address:hiz@Zeliger.com](mailto:address:hiz@Zeliger.com) (Harold I. Z.)

and 42% of women with CFS also have MCS, while between 13% and 88% of people with MCS also have CFS [8, 9, 10]. The present study was undertaken to ascertain if either of the two conditions, MCS or CFS preceded the other in individuals affected with both conditions.

## 2. Methods

An online survey of patients suffering from MCS and CFS was undertaken. 2,200 individuals from the United States, Canada and Western Europe suffering from one or both of these conditions were solicited to respond to a questionnaire that asked respondents to give their gender, age category (under 40,40-60, over 60), which of the conditions they suffered from and for those suffering from both conditions, which one came first.

Statistical analysis of the data to determine which occurs first, MCS or CFS, was carried out using a McNemar's test, a Chi-square test for paired data [1 I]. Adopting McNemar's Test to our study, we calculated the following:  $(CS\ First - CF\ First) / (CS\ First + CF\ First) = Chi\text{-square with } 1\ df$ . The critical value for Chi-square with 1 df and an alpha of 0.05 is 3.84.

## 3. Results

Of the 2,200 who were solicited, 544 responded. Of these, 315 (58%) were co-morbid with both conditions. Of these co-morbid individuals, 170 cases were reported in which MCS occurred first and 145 cases where CFS occurred first. Though overall 54% of those individuals suffered the onset of MCS first, and 46% reported CFS first, the differences are small and statistically insignificant (Chi squared = 1.98m p-value = 0.17. Half of the respondents of all three age groups and both genders reported getting ill with MCS first, while half reported the onset of CFS first. The results broken down by age groups and gender are shown in table 1.

## 4. Discussion

Our finding that 58% of people with one or the other condition are co-morbid is consistent with other published results that show co-morbidities of MCS and CFS to range between 42% and 88% [9]. Both MCS and CFS have strong immunological and neurological impacts on those afflicted with them [10]. Though the exact mechanism(s) for the onset of these diseases is/are unknown, it is to be anticipated that similar pathways may be operating given the high degree of both co-morbidity and overlap of symptoms that affect multiple systems of the body [2,9]. Our results showing that neither disease is more likely to precede the other in co-morbid cases may be useful for testing hypotheses about the mechanisms causing them,

particularly with respect to common pathways reflected in their high level of co-occurrence. Our results here are consistent with other studies in which it has been shown that individuals with two co-morbid environmental diseases, e.g., type 2 diabetes and hypertension, are just as likely to become ill with the either one [12,13]. Unifying explanations for this phenomenon are offered by a consideration of the mechanism of onset or exogenous lipophilic chemical promoted environmental disease, the timing of their onset and the co-morbidities of these diseases.

**Table 1.** Numbers and percents of individuals with both MCS and CFS reporting MCS onset first and CFS onset first.

	MCS First	CFS First	Chi-square
	n	n	
	%	%	
All Respondents	170	145	
	54	46	
Under 40	14	17	0.29
Female	45	55	0.82
Under 40	7	4	
Male	64	36	1.51
40-60	82	67	
Female	55	45	1.32
40-60	22	15	
Male	59	41	0
Over 60	35	35	
Female	50	50	0.82
Over 60	7	4	
Male	64	36	

Both MCS and CFS are known to be triggered by environmental pollutants [2,3]. It has been known since 2003 that exposures to mixtures of lipophilic and hydrophilic chemicals trigger low level responses, enhanced toxic effects and attacks at organs and systems not known to be targeted by the individual components of the mixtures [14]. Hydrophilic chemicals, though generally more toxic than lipophilic species, have only limited ability to penetrate the body's lipophilic barriers. In mixtures of lipophiles and hydrophiles, the hydrophiles dissolve into the lipophiles and are carried through the body's lipophilic membranes. This mechanism is identical with the use of lipophilic additives to facilitate the absorption of hydrophilic pharmaceuticals. It has been further shown that specific mixtures of lipophilic and hydrophilic species act as single agents and are site-specific attackers in the human body [15]. The specific mixtures of disease causation of MCS and CFS remain unknown. Given the presence of numerous mixtures of toxic chemicals in the everyday environment, and the fact that different people are exposed to different environments, it is plausible that some individuals will be exposed to mixtures that favor the causation of MCS while others will be exposed to mixtures that favor the causation of CFS.

MCS and CFS are both primarily late-onset diseases that are more common with increasing age. This is analogous with the

late onset of other environmental diseases including type 2 diabetes, cardiovascular diseases, neurodegenerative diseases and cancer which has been attributed to sequential absorption of lipophilic and hydrophilic species and the body's ability to rid itself of these toxicants [12]. Upon absorption, the body immediately acts to rid itself of exogenous toxins via elimination and metabolism. Whereas hydrophilic chemicals are rapidly eliminated, lipophilic species are longer lived in the body and may persist for days to weeks, as is the case for low molecular weight hydrocarbons such as hexane, benzene, toluene and xylene; and semi-volatile organic compounds such as polynuclear aromatic hydrocarbons, phthalates and bisphenol-A; to decades for persistent organic pollutants such as polychlorinated biphenyls (PCBs), dioxins and chlorinated pesticides [15]. Given this dynamic, the total lipophilic load is critical to the body's propensity to absorb hydrophilic species when exposure to these compounds occurs. It has been shown, for example, that dose-response relationships exist between serum levels of persistent organic pollutants and the onset of type 2 diabetes [16], and between serum levels polynuclear aromatic hydrocarbons and the onset of cancer [17]. Analogous relationships between body loads of lipophilic chemicals and the onset of MCS or CFS are hypothesized to be prevalent. Both MCS and CFS have co-morbidities with several other environmental diseases. MCS is co-morbid with immunological, cardiovascular, musculoskeletal, gastrointestinal and neurological diseases [18]. CFS is co-morbid with neurological, musculoskeletal and gastrointestinal diseases [19]. Virtually all environmental diseases have numerous co-morbidities with other environmental diseases [12].

The above considerations suggest prevention and treatment options for individuals affected with MCS or CFS. These include limiting exposures to sources of lipophilic chemicals: polluted air; tobacco smoke from primary (smoking), secondary (inhaling of others' tobacco smoke, and tertiary (inhalation of fumes emanating from clothing and furniture fabrics that absorb and release polynuclear aromatic hydrocarbons from tobacco smoke); following a Mediterranean type diet that limits the ingestion of foods with high levels of animal fats and processing chemicals (hydrocarbon solvents and preservatives); and limiting the use of polystyrene, polycarbonate and polyvinylchloride plastics for food storage and consumption (sources of styrene monomer, bisphenol-A and phthalates [20]. It is noteworthy that taking such preventative measures can also lower the incidences of other environmental diseases.

## 5. Conclusion

To our knowledge, this is the first time that an attempt has

been made to see whether MCS precedes CFS, or vice versa.

The results presented demonstrate that there is no significant bias with respect to either condition preceding the other in cases of co-morbidity. Both MCS and CFS are environmental diseases with onset mechanisms that are hypothesized to be similar to those for the onset of other environmental diseases with which they are co-morbid. Accordingly, preventative measures can be taken to lower the incidences of both diseases.

## Acknowledgment

We thank Lourdes Salvador for her help in the preparation and distribution of the survey.

## References

- [1] Caress SM, Steinemann AC. Asthma and chemical hypersensitivity: prevalence, etiology, and age of onset. *Toxicol Ind Health* 2009; 25:71-78.
- [2] Brown MM, Jason LA. Functioning in individuals with chronic fatigue syndrome: increased impairment with co-occurring multiple chemical sensitivity and fibromyalgia. *Dyn Med* 2007; 6: 6.
- [3] De Luca C, Raskovic D, Pacifico V, Thai JC, Korkina L. The search for reliable biomarkers of disease in multiple chemical sensitivity and other environmental intolerances. *Int J Environ Res Public Health* 2011; 8(7):2770-97.
- [4] Kreutzer R, Neutra RR, Lashuay N. Prevalence of people reporting sensitivities to chemicals in a population-based study. *Am J Epidemiol* 1999; 150(1):1-12.
- [5] Centers for Disease Control. The 1994 case definition: CFS. <http://www.cdc.gov/cfs/case-definition11994.html> (accessed December 9, 2013).
- [6] Johnson S, Brenu EW, Staines D, Marshall-Gradisnik S. The prevalence of chronic fatigue syndrome/ myalgic encephalomyelitis: a meta-analysis. *Clinical Epidemiol* 2013; 20 I 3(5): 105- I 10.
- [7] Underhill R. Chronic fatigue syndrome in children and adolescents. *New Jersey Chronic Fatigue Syndrome Assoc.* <http://njcfsa.org/FACTPEDLhtml> (accessed December 12, 2013).
- [8] Ciccione DS, Natelson BH. Comorbid illness in women with chronic fatigue syndrome: A test of the single syndrome hypothesis. *Psychosom Med* 2003; 65:268-75.
- [9] Jason LA, Taylor RR, Kennedy CL. Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in community-based sample of persons with chronic fatigue-like symptoms. *Psychosom Med* 2000; 62(5):655-63.
- [10] Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities. *Arch Int Med* 1994; 154(18):2049-53.
- [11] McNemar Q. Note on the sampling error of the difference between correlated proportions or percentages. *Psychometrika* 1947; 12(2):153-57.

- [12] Zeliger HI. Co-morbidities of environmental diseases: A common cause. *Interdiscip Toxicol*2014; 7(3): 10 1-106.
- [13] Sowers JR, Epstein M. Diabetes mellitus and associated hypertension, vascular disease, and nephropathy. *Hypertension* 1995; 26:869-79.
- [14] Zeliger HI. Toxic effects of chemical mixtures. *Arch Environ Health* 2003; 58 (1): 23-29.
- [15] Zeliger HI. *Human toxicology of chemical mixtures*, 2nd ed., Elsevier, London.
- [16] Lee DH, Lee IK, Song K, Steffes M, Toscano W, Baker BA, Jacobs DR Jr. A strong dose-response relationship between serum concentrations of persistent organic pollutants and diabetes. *Diabetes Care* 2006; 29(7): 1638-44.
- [17] Law MR, Morris J, Watt HC, Wald NJ. The dose-response relationship between cigarette consumption, biochemical markers and risk of lung cancer. *Br J Cancer* 1997; 75(11):1690-93.
- [18] Zeliger HI, Pan Y, Rea WJ. Predicting co-morbidities in chemically sensitive individuals from exhaled breath analysis. *Interdiscip Toxicol*2012; 5(3): 123-26.
- [19] Aaron LA, Herrel R, Ashton S, Belcourt M, Schmaling K, Goldberg J, Buchwald D. Comorbid clinical conditions in chronic fatigue. *J Gen Intern Med* 2001; 16: 24- 31.