

Prevalence and Overlap of Chronic Fatigue Syndrome and Fibromyalgia Syndrome Among 100 New Patients with Multiple Chemical Sensitivity Syndrome

Albert Donnay, MHS
Grace Ziem, MD, DrPH

SUMMARY. Background: Several studies have reported on extensive two-way overlaps found among chronic fatigue syndrome (CFS), fibromyalgia syndrome (FMS) and multiple chemical sensitivity syndrome (MCS) but none have yet reported on the overlap of all three. This study assesses the prevalence of pure MCS, MCS-CFS, MCS-FMS and the overlap of all three among 100 consecutive new patients evaluated for MCS in a private practice specializing in occupational and environmental medicine.

Methods: Sixty-eight females and 32 males diagnosed with MCS—

Albert Donnay is President of MCS Referral & Resources, Inc.

Grace Ziem maintains a private practice specializing in chemical injury and is the co-founder of MCS Referral & Resources, Inc.

Address correspondence to: Albert Donnay, 508 Westgate Road, Baltimore, MD 21229.

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based on a medical history of multiple chronic symptoms in multiple organs triggered by multiple chemical exposures at or below previously tolerated levels—were also evaluated for CFS and FMS using the diagnostic criteria of the US Centers for Disease Control and the American College of Rheumatology, respectively.

Results: Eighty-eight percent of the 100 MCS patients met criteria for CFS, 49% met criteria for FMS, and 47% met both. Slightly more male than female MCS patients had CFS: 91% vs. 87%; while FMS was more than twice as common among female MCS patients: 59% vs. 28%. The majority of women, 56%, met criteria for all three disorders, and an additional 31% had both MCS and CFS. This pattern was reversed in men, only 28% of whom had all three, compared to 63% with MCS and CFS but no FMS. MCS alone was diagnosed in only 10% of the women and 9% of the men. Even rarer was the overlap of MCS and FMS without any CFS, found in just 2 women.

Conclusions: At least in this clinic population, MCS seldom occurs alone. The enormous range of diagnostic overlaps reported here and in previous studies of various overlaps among CFS, FMS and MCS highlights the need to screen for all three disorders in studies of any one and to report results in these terms. We recommend this be made standard practice in both clinical settings and research protocols. [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-342-9678. E-mail address: geinfo@haworthpressinc.com <Website: <http://www.haworthpressinc.com>>]

KEYWORDS. Fatigue syndrome, chronic; fibromyalgia, multiple chemical sensitivity, prevalence, case series

INTRODUCTION

This study evaluates the overall, gender- and age-specific prevalence of chronic fatigue syndrome (CFS), fibromyalgia syndrome (FMS) and their overlap among 100 adults seen for evaluation of multiple chemical sensitivity syndrome (MCS) at a private clinic specializing in occupational and environmental medicine. While others have previously reported finding extensive 2-way overlaps among these disorders in various clinic populations, this study is the first to also examine their 3-way overlap.

CFS, FMS and MCS are all relatively recently defined chronic disorders that share many of the same clinical signs, symptoms, and demographics but are usually attributed to different causes. CFS often appears to evolve from flu-like symptoms, FMS from a physical injury or surgery, and MCS from chemical exposure, but their many similarities suggest they may share underlying mechanisms (1). All may begin gradually or suddenly, usually between

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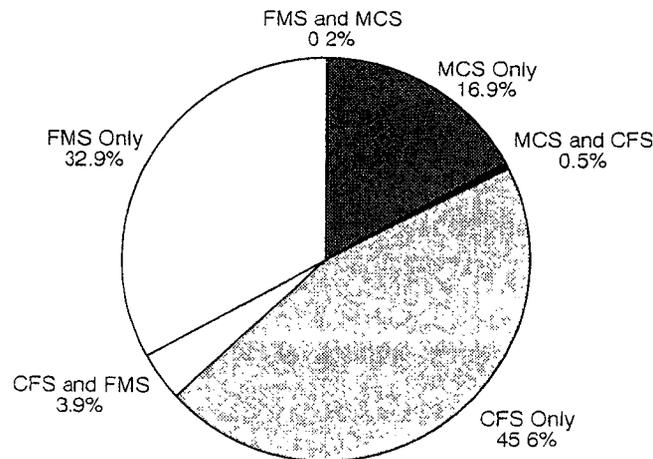
the ages of 20 to 50, and are most common in women. All three also are characterized by a diverse range of relatively common symptoms in the central nervous system and other organs that may be triggered by a wide variety of stressors—chemical, biological, physical, environmental and/or psychosocial—at or below previously tolerated levels.

Given these similarities, it is not surprising that many CFS, FMS, and MCS researchers have reported finding similar abnormalities in a wide variety of physiological and psychological parameters, including sleep (2-4), immune response (5-7), neuro-endocrine function (1,8,9), neurocognitive capacity (10-12), cerebral blood flow (13-15), and cardiac output (16-18).

But since the first formal definitions were published of MCS in 1987 (19), CFS in 1988 (20), and FMS in 1990 (21)—none of which require exclusion of any of the others—few researchers have studied their various overlaps or controlled for these when screening for cases and controls. Among 2167 peer-reviewed articles, editorials and letters published on these disorders in the last decade, only 4.6% mention any overlap, and 85% of these address only the overlap between CFS and FMS (Figure 1).

The first study to discuss all three, by Buchwald and Garrity (22), found two-thirds (67%) of both their FMS and CFS study groups complained of chemical sensitivity, making these by far the largest overlapping subsets. A much smaller but still substantial quarter (24%-25%) of both FMS and MCS

FIGURE 1. Articles, Editorials and Letters Indexed by the National Library of Medicine on CFS, FMS and MCS, 1987 to 1997, Combined n = 2,167



Only 3 references (not shown) address all three of CFS, FMS and MCS

groups complained of chronic fatigue lasting longer than 6 months that caused a 50% or more reduction in daily activity; while one fifth (19%-23%) of the CFS and MCS groups reported myalgia and arthralgia (physical exams were not done). Unfortunately, neither they nor any one else has reported on the three-way overlap that is most likely also present to a significant degree (23). The objective of this study is to determine the prevalence of this 3-way overlap as well as the rates of pure MCS (MCS only), MCS-CFS, and MCS-FMS in an MCS clinic population.

METHODS

One hundred new adult patients (68 F and 32 M) consecutively seen from January 1996 to January 1998 in Dr. Ziem's private medical practice with a diagnosis of MCS were also evaluated upon their initial visit for CFS and FMS. MCS was diagnosed according to criteria common to the published criteria of Cullen (19) and others (24): a minimum 6 month history of multiple persistent or recurring symptoms in multiple organs triggered by multiple exposures to multiple chemicals—inhaled, ingested and/or absorbed at or below levels previously tolerated—which cannot be fully explained by any other multi-system disorders like lupus or the inherited porphyrias.

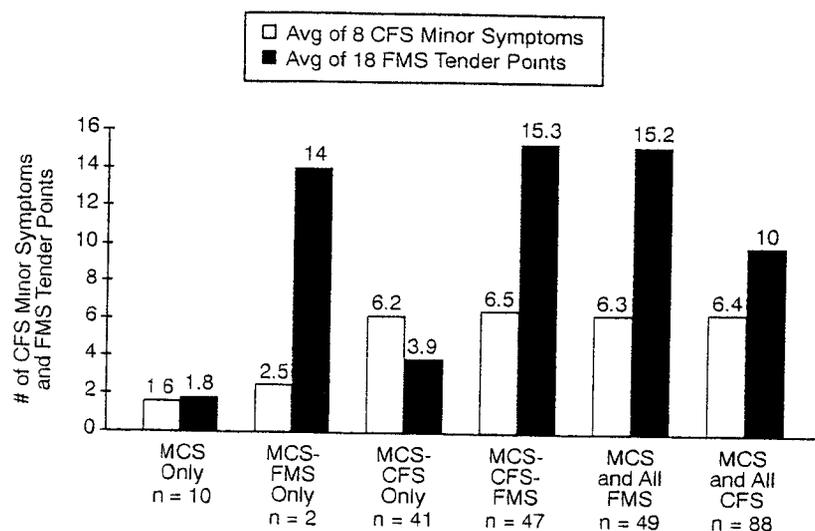
CFS was diagnosed by the criteria of the US Centers for Disease Control (25) and FMS by those of the American College of Rheumatology (21), including its tender point criteria. But given the clinical setting in which these diagnoses were made, the exclusion criteria included in the CFS research definition were not used in order that the full extent of the overlap with MCS could be assessed. Data retrieved for the study included the number of secondary criteria met for CFS (8 maximum with at least 4 required for diagnosis) and the number of FMS tender points demonstrating pain upon manual palpation (18 maximum with at least 11 required for diagnosis), as well as basic demographics—gender and age at time of evaluation.

Diagnostic data were then evaluated by gender and age (youngest half vs. oldest) to determine the relative prevalence of each of four MCS subtypes (MCS only, MCS-CFS, MCS-FMS and MCS-CFS-FMS) and to see if any trends or significant associations were evident.

RESULTS

Of the 100 MCS patients, 88% met the criteria for CFS (the MCS-All CFS subset) with all the major and an average of 6.4 of the 8 minor criteria, and 49% met the criteria for FMS with pain in an average of 15.2 of the 18 tender points (Figure 2). In comparison, the 12% of MCS cases who did not meet the

FIGURE 2. MCS Subtypes by Average Number of CFS Minor Symptoms and FMS Tender Points

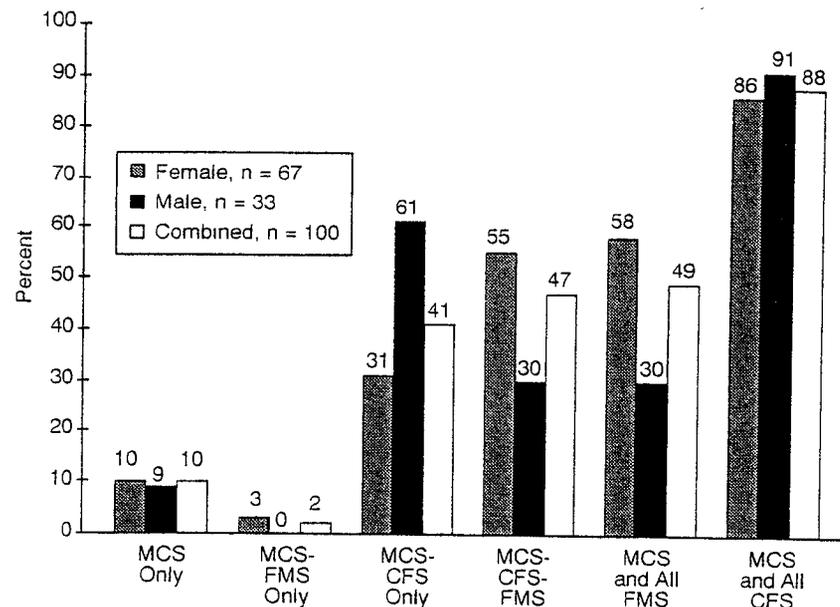


definition of CFS (the MCS only and MCS-FMS only subsets) reported an average 1.75 minor criteria, while the 51% who did not meet the definition of FMS (the MCS only and MCS-CFS only subsets) reported an average of 3.26 painful tender points. Significant differences are seen in the number of CFS symptoms among the MCS-FMS only subset (without CFS) versus the clearly sicker MCS-All FMS subset, and similarly, in the number of FMS tender points among MCS-CFS only subset versus the MCS-All CFS.

A breakdown in the relative prevalence of MCS subtypes by gender is shown in Figure 3. The extraordinarily high rate of CFS overall (the MCS-All CFS subset) was even slightly higher among male MCS patients: 91% vs. 87%. In contrast, FMS was twice as common overall (the MCS-All FMS subset) among the women with MCS: 59% vs. 28%. Among women, 56% met criteria for all three disorders, and an additional 31% had MCS and CFS alone. This pattern was reversed in men, with 63% having both MCS and CFS alone and only 28% having all three. The diagnosis of MCS only was relatively rare, occurring in only 10% of women and 9% of men.

Even rarer was the overlap of MCS and FMS only (without any CFS), which was found in just 2 women and no men. While FMS was almost always accompanied by CFS in these MCS patients regardless of gender (in 100% of male FMS cases and 95% of female cases), only 31% of the male CFS cases were associated with FMS compared with 65% of the female ones.

FIGURE 3. MCS Subtypes by Gender and Combined



When assessed by age, there were no significant differences between the medians of any category, which ranged from 42 for those with MCS-CFS alone to 50 for those with pure MCS. This small variation was due entirely to the men (median age 42), whose younger half had no cases of pure MCS (compared to 3 in the older half) but 50% more cases of MCS and CFS alone (12 to 8). Among women, there was no difference between the older and younger halves (median age 43) in the relative prevalence of any category.

Unexpectedly, the number of secondary CFS symptoms reported declined 20% in older men and 9% in older women, while the average number of FMS tender points declined only negligibly (1% in men and 5% in women).

DISCUSSION

Among the 100 cases we reviewed from this private practice, MCS seldom occurred alone. Almost all (88%) met current diagnostic criteria for CFS and half (49%) also had FMS. On average, MCS patients with CFS and/or FMS also had more secondary CFS symptoms (6.4) and/or FMS tender points (15.2), respectively, than those reported in unscreened CFS and FMS clinic

populations, suggesting that these disorders may be more severe when comorbid with MCS.

Most significantly, almost half the total (47%) met criteria for all three disorders but this included just 1/3 of the men compared to 2/3 of the women. This surprising difference was not due at all to CFS, which unexpectedly was slightly more prevalent among male than female MCS patients, but rather to FMS, which was twice as prevalent in women. In all but two MCS cases, both women, FMS also overlapped with CFS. The 96% rate of CFS among those with FMS is almost four times the 25% reported by Buchwald and Garrity (22) and more than twice the 42% overlap reported by Hudson et al. (26) in a study of FMS clinic patients.

The overlap of MCS with All CFS in this private practice was 20% greater, and the overlap with All FMS 20% less, than the 67% reported for both by Buchwald and Garrity (22). These overlaps also are an order of magnitude greater than the 7% MCS-CFS overlap reported in the largest study to date of Gulf War veterans (27).

We can only speculate on the reasons for these differences, but they most likely involve both the choice of diagnostic criteria and study populations, since MCS clinic patients with CFS and/or FMS appear sicker than CFS and/or FMS clinic patients overall, based on their average number of secondary CFS symptoms and FMS tender points.

The MCS-FMS overlap, however, is almost identical to the 55% rate of MCS among FMS clinic patients reported by Slotkoff, Radulovic and Clauw (28), who created a new and less restrictive definition of MCS that did not require symptoms in *multiple* organs in response to any single chemical exposure. Although Slotkoff et al. concluded that MCS is "an additional allied spectrum of FM," this study shows that FMS is no less a spectrum of MCS. The overlay of cardinal symptoms is even greater: 90% of the FMS patients in their study reported some degree of chemical sensitivity and 90% of the MCS patients in this study (all except those in the MCS only subset) reported some muscle and joint pain.

Although perhaps only a coincidence but possibly partly a reflection of predisposing genetic differences or immune activation (5), chemical sensitivity also has been found to overlap with allergy by 50% and vice versa, in a telephone survey of over 1000 randomly selected rural North Carolinian adults (29).

The enormous range of these diagnostic overlaps highlights the need in any study of CFS, FMS or MCS to screen for all three disorders using published criteria and to report results in terms of their various overlaps. We recommend this be made standard practice in both clinical settings and research protocols and offer a 10-item questionnaire developed for this purpose (30).

To improve the early detection, treatment and prevention of these disorders, we recommend that patients diagnosed with CFS, FMS or MCS in clinical or research settings be followed carefully to determine the relative order in which the hallmark symptoms of chemical sensitivity, chronic fatigue, and fibromyalgia appear as well as the kinds of events (illness, injury, toxic exposure, etc.) associated with their onset. A short questionnaire developed for this purpose that allows the plotting of these developments on a timeline also is available from the authors.

We suggest that in many of these cases, the diagnoses of CFS, FMS and MCS may simply reflect different aspects of a common underlying medical condition, which is how the cardinal symptoms of these disorders—chronic fatigue, systemic myalgias/artralgias, and chemical (i.e., drug, alcohol and food) sensitivities—were recognized in medicine for more than a century before they began to be diagnosed separately in the late 1980s. Drs. Eugene Buchot in Paris, Edward Van Deusen in Michigan and George Miller Beard in New York independently described all three as hallmark symptoms of neurasthenia in 1858 (31), 1869 (32), and 1880 (33), respectively. In the twentieth century, Dr. Theron Randolph first recognized their overlap in 1945 as part of a syndrome associated with food intolerances (34) and sensitivity to petroleum and pine products (35). He called this "allergic toxemia" specifically to distinguish it from neurasthenia, which since the turn of the century—post-Freud (36)—had been routinely dismissed as psychogenic.

Given the relative rarity of pure MCS cases (just as pure CFS and pure FMS are also a minority), we also recommend that greater emphasis be placed in research and physician education on the more common and usually more severe overlapping cases, especially the 3-way neurasthenic-like overlap which appears to be the most common. Pure cases should still be studied in order to identify any biomarkers that may truly distinguish between them, but these need to be checked in each category of possible overlap. Some biomarkers currently being studied in isolation, for example, such as abnormal SPECT scans, may turn out to be more diagnostic of the 3-way overlap than any one of these disorders.

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