Multiple Chemical Sensitivity and Chronic Fatigue Syndrome in British Gulf War Veterans

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The objective of this study was to measure the prevalence of multiple chemical sensitivity (MCS) and chronic fatigue syndrome (CFS) in British Gulf War veterans and to investigate their association with reported exposures and psychologic morbidity. In 1997–1998, the authors undertook a cross-sectional survey of three cohorts of British military personnel comprising Gulf veterans ($n = 3,531$), those who had served in Bosnia ($n = 2,050$), and those serving during the Gulf War but not deployed there (Era cohort, $n = 2,614$). MCS and CFS were defined according to operational criteria. The prevalence of MCS in the Gulf, Bosnia, and Era cohorts was 1.3%, 0.3%, and 0.2%, respectively. For CFS, the prevalence was 2.1% (Gulf cohort), 0.7% (Bosnia cohort), and 1.8% (Era cohort). In Gulf veterans, MCS was strongly associated with exposure to pesticides (adjusted odds ratio = 12.3, 95% confidence interval: 5.1, 30.0). Both syndromes were associated with high levels of psychologic morbidity. These findings suggest that CFS and MCS account for some of the medically unexplained illnesses reported by veterans after deployment to the Gulf. MCS was particularly associated with Gulf deployment and self-reported exposure to pesticides, findings that merit further exploration given the controversial status of this diagnosis and the potential for recall bias in a questionnaire survey. *Am J Epidemiol* 2001;153:604–9.

fatigue syndrome, chronic; multiple chemical sensitivity; occupational exposure; Persian Gulf syndrome

Since the end of the Gulf War, many veterans have developed illnesses that they have attributed to their military service. Of particular concern is the possibility that exposure to biological, chemical, or other environmental hazards may be responsible. While it is now clear that Gulf veterans report higher rates of symptoms than do service personnel who were not deployed in the Gulf (1–6), the existence of a specific "Gulf War syndrome" has not been conclusively demonstrated (1, 2, 4). At the same time, there have been numerous anecdotal reports of veterans presenting with medically unexplained, multisymptom conditions, such as chronic fatigue syndrome (CFS) and multiple chemical sensitivity (MCS).

MCS is characterized by the reporting of a wide variety of symptoms that are attributed to chemical exposure or sensitivity in the absence of accompanying physical signs or biomedical test abnormalities (7). Despite a lack of convincing evidence, abnormalities of the central nervous system or immune dysfunction have been implicated in its etiology. The status of MCS is viewed with scepticism by many, and several authoritative reports have questioned its validity (8–10). MCS has yet to make a significant impact in the United Kingdom. This is in sharp contrast to the situation in the United States, Canada, and Germany. Even though the diagnosis remains highly controversial in professional circles in these countries, it is in widespread use. A recent epidemiologic study reported that 6 percent of a surveyed population had been given a diagnosis of MCS by their physician (11).

In this paper, we report the prevalence of MCS and CFS, according to operational criteria, in the British Gulf War veteran population. The relations between these diagnoses and various exposures are explored, as are their associations with psychologic morbidity.

MATERIALS AND METHODS

The sample was obtained from a cross-sectional postal survey, conducted in 1997–1998, comparing three cohorts of British military personnel: veterans deployed to the Gulf War, veterans who served in the first four regiments deployed to the Bosnia conflict, and veterans in active service on January 1, 1991, but not deployed to the Gulf War (Era cohort). Respondents who had served in both the Gulf War and the Bosnia conflict were defined as veterans of the Gulf War and included in that cohort. Details of stratification, methods of selection, and tracing are described in an earlier paper (3). After three mailings, the overall response rate was 65.1 per-

TABLE 1. Prevalence of medically unexplained syndromes by deployment, British military personnel, 1997–1998

	Gulf (n = 3,531)		Bosnia (n = 2,050)		Era (n = 2,614)	
	Frequency (%)	95% CI*	Frequency (%)	95% CI	Frequency (%)	95% CI
Chronic fatigue syndrome	2.1	1.6, 2.6	0.7	0.4, 1.2	1.8	1.3, 2.4
Multiple chemical sensitivity	1.3	1.0, 1.7	0.3	0.1, 0.6	0.2	0.1, 0.4

* CI, confidence interval.

cent (8,195/12,592), rising to 70.0 percent (n = 3,531/5,046) for those serving in the Gulf. In addition to demographic details and exposure history (29 items), the questionnaire contained several measures of current health status, including a checklist of 50 symptoms (12) and 39 medical disorders, the General Health Questionnaire (13) (a measure of psychiatric morbidity), a fatigue questionnaire (14), the Short Form-36 (SF-36, a health status questionnaire) (15), and an approximation of posttraumatic stress disorder, which we refer to as posttraumatic stress reaction (16). Included in the list of medical disorders were questions asking whether, after active service, participants had suffered from 1) CFS (myalgic encephalomyelitis) or 2) MCS/environmental illness.

To estimate prevalence numbers, the Centers for Disease Control and Prevention (CDC) diagnosis of CFS (17) was derived from a combination of "caseness" according to the fatigue questionnaire and the SF-36 measure of functional disability. This method of case identification has been used in previous population studies of CFS (18). For MCS, cases were defined by the operational criteria used by Simon et al. (19) in a case-control study of the illness. These criteria require that symptoms are reported in at least three organ systems, including the central nervous system, for a duration of 3 months or more and that there is reported sensitivity to four or more substances from a list of 14, including fresh paint, hair spray, and solvent fumes. The present questionnaire included 11 substances derived from a shortened measure of symptoms of possible chemical sensitivity (20).

Data were analyzed using STATA (version 5.0) (21). The prevalence of both illnesses was calculated for the three cohorts—Gulf War, Bosnia, and Era. For the Gulf War cohort, veterans fulfilling the criteria for CFS and MCS (cases) were compared with those self-reporting the diagnosis. Proportions of exposures and health outcomes were compared in those defined as cases, using odds ratios and 95

percent confidence intervals. Logistic regression analysis was used to control for potential confounders.

RESULTS

Both CFS and MCS were more frequent in the Gulf cohort (tables 1 and 2), although the prevalence of CFS in the Era cohort was not significantly different from that in the Gulf War cohort.

Further analyses were restricted to the Gulf War veterans. Demographic characteristics of the veterans who fulfilled the criteria for CFS and MCS are shown in table 3. For CFS, cases did not differ from noncases in terms of gender or age or by primary duty. However, non-White veterans were more likely to be cases, as were those who were separated, divorced, or widowed and those with lower educational attainment. Current unemployment, being discharged from the service, and being of nonofficer rank were also associated with being a case. For MCS, educational attainment was the only demographic characteristic for which there was a significant association, with those achieving a lower educational attainment more likely to be cases. Again, current unemployment and being discharged from the service were also associated with the diagnosis.

For veterans who fulfilled case definitions, seven of the 76 CFS cases (9.6 percent) also met the criteria for MCS. Conversely, seven of 46 (15.2 percent) MCS cases met the criteria for CFS. Of the 113 who self-reported CFS, 12 (10.6 percent) fulfilled operational criteria for CFS. Twelve (16.4 percent) of the 73 operationally defined cases of CFS also self-reported the diagnosis. Of the 27 who self-reported MCS, eight (29.6 percent) fulfilled operational criteria of MCS. Eight (17.4 percent) of the 46 operationally defined cases of MCS also self-reported the diagnosis. We compared self-reported diagnoses with caseness ascertained by operational criteria using kappa

TABLE 2. Comparison of medically unexplained syndrome prevalences, British military personnel, 1997–1998

	Gulf vs. Bosnia				Gulf vs. Era			
	Unadjusted OR*	95% CI*	Adjusted OR†	95% CI	Unadjusted OR	95% CI	Adjusted OR†	95% CI
Chronic fatigue syndrome	3.1	1.7, 5.4	2.3	1.2, 4.3	1.2	0.8, 1.7	1.2	0.8, 1.8
Multiple chemical sensitivity	4.5	1.9, 10.5	4.5	1.7, 11.8	6.9	2.7, 17.4	7.2	2.8, 18.2

* OR, odds ratio; CI, confidence interval.
† Controlled for gender, age, marital status, education, rank, and employment status on follow-up.

TABLE 3. Characteristics of Gulf veterans with medically unexplained syndromes, British military personnel, 1997–1998

	CFS*			MCS*		
	No. (% with CFS)	OR*	95% CI*	No. (% with MCS)	OR	95% CI
Gender						
Male	3,295 (2.1)			3,295 (1.3)		
Female	236 (2.1)	1.0	0.4, 2.6	236 (1.7)	1.3	0.5, 3.8
Age (years)						
<25	4 (0.0)			4 (0.0)		
25–29	986 (2.1)	1.0		986 (1.2)	1.0	
30–34	1,080 (2.1)	1.0	0.6, 1.8	1,080 (1.3)	1.1	0.5, 2.3
35–39	707 (1.4)	0.7	0.3, 1.4	707 (1.0)	0.8	0.3, 2.1
≥40	754 (2.5)	1.2	0.6, 2.2	754 (1.7)	1.4	0.7, 3.1
Ethnicity						
White	3,480 (2.0)			3,480 (1.3)		
Non-White	41 (7.3)	3.9	1.2, 13.0	41 (0.0)		
Marital status						
Married or living with partner	2,627 (1.7)	1.0		2,627 (1.3)	1.0	
Never married	565 (2.3)	1.4	0.7, 2.5	565 (0.9)	0.7	0.3, 1.8
Separated, divorced, or widowed	317 (4.7)	2.8	1.6, 5.2	317 (2.2)	1.7	0.8, 3.9
Education†						
Below "O" level	645 (3.6)	2.7	1.3, 5.6	645 (2.5)	3.1	1.2, 7.9
"O" level	2,051 (1.5)	1.1	0.5, 2.2	2,051 (1.1)	1.8	0.5, 3.2
"A" level	730 (1.4)	1.0		730 (0.8)	1.0	
Currently employed						
Yes	3,289 (1.3)			3,289 (0.9)		
No	174 (16.1)	14.8	8.8, 24.9	174 (9.2)	11.4	6.1, 21.4
Currently serving in the military						
Yes	1,966 (1.1)			1,966 (0.4)		
No	1,551 (3.2)	3.1	1.8, 5.2	1,551 (2.4)	6.2	2.9, 13.2
Rank						
Officer	449 (0.2)			449 (0.4)		
Other ranks	1,551 (2.3)	10.7	1.5, 77.6	3,079 (1.4)	3.2	0.8, 13.4
Duty in Gulf						
Combat	685 (2.0)	1.0		685 (2.0)	1.0	
Signals	235 (2.6)	1.3	0.5, 3.3	235 (0.8)	0.4	0.1, 1.8
Medical	383 (1.6)	0.8	0.3, 2.0	383 (1.3)	0.6	0.2, 1.8
Logistics	874 (2.8)	1.4	0.7, 2.6	874 (1.1)	0.6	0.2, 1.2
Staff	112 (0.0)			112 (0.0)		
Other	741 (1.1)	0.5	0.2, 1.2	741 (0.7)	0.3	0.1, 0.9

* CFS, chronic fatigue syndrome; MCS, multiple chemical sensitivity; OR, odds ratio; CI, confidence interval.
† "O" level, examinations usually taken at age 16 years and required before "A" level; "A" level, examinations usually taken at age 18 years and required for entry into a university.

statistics. For CFS, agreement was 0.11 ($p < 0.001$), and for MCS, it was 0.21 ($p < 0.001$), indicating levels of agreement little above chance.

For exposures, we found that being a CFS case was most strongly associated with combat-related injury (table 4). There was also an association with exposure to the explosion of SCUD missiles, nearby artillery, chemical alarms, witnessing a person's death, maimed soldiers, and the burning of rubbish/feces. For MCS (table 5), cases were more likely to be associated with the majority of exposures listed.

The strength of association with exposures was generally greater, and this was markedly the case for exposure to pesticides used either personally or on clothing/bedding. On stratifying for belief in the presence of MCS (self-report), the association with pesticides remained significant ($p = 0.014$). Both diagnoses were associated with the psychologic health outcomes (tables 6 and 7). Approaching 100 percent of subjects with CFS or MCS were cases on the General Health Questionnaire. MCS had a particularly strong association with posttraumatic stress reaction.

TABLE 4.   Association between reported exposures and chronic fatigue syndrome in Gulf veterans, British military personnel, 1997–1998

Chronic fatigue syndrome	Unadjusted OR*	95% CI*	Adjusted OR†	95% CI
Diesel or petrochemical fumes	1.2	0.6, 2.3	1.4	0.6, 3.0
NBC* suits	1.6	0.8, 3.2	1.5	0.6, 3.4
Pyridostigmine bromide	1.6	0.8, 3.2	1.5	0.7, 3.4
Exhaust from heaters	1.3	0.7, 2.3	1.4	0.7, 2.6
Smoke from oil fires	0.9	0.5, 1.4	1.1	0.6, 2.0
Hear chemical alarms	2.6	1.3, 5.0	2.5	1.2, 5.3
Personal pesticides	1.2	0.7, 2.1	1.0	0.6, 1.8
Local food	0.8	0.5, 1.4	0.9	0.5, 1.6
Burning rubbish/feces	2.1	1.2, 3.7	2.0	1.0, 3.4
Diesel on skin	2.1	1.2, 3.6	1.8	1.0, 3.5
Dismembered bodies	1.9	1.1, 3.4	1.6	0.8, 3.0
Other paints or solvents	1.3	0.8, 2.2	1.4	0.8, 2.5
Dead animals	1.2	0.8, 2.0	1.3	0.7, 2.2
POWs*	1.3	0.8, 2.1	1.4	0.8, 2.5
Maimed soldiers	2.1	1.3, 3.5	2.0	1.2, 3.6
Pesticides on clothing	1.4	0.9, 2.2	1.2	0.7, 2.0
Chemical/nerve gas attack	1.7	0.9, 3.4	1.5	0.7, 3.1
Mustard gas	2.5	0.9, 7.1	1.4	0.4, 4.6
Combat-related injury	6.1	3.6, 10.3	4.1	2.2, 7.7
Witness anyone dying	2.3	1.4, 3.6	2.2	1.3, 3.8
SCUD missile explosion	2.2	1.4, 3.6	2.6	1.5, 4.6
Small-arms fire	1.3	0.8, 2.1	1.3	0.8, 2.3
Artillery close by	1.8	1.2, 2.9	2.4	1.4, 4.1

* OR, odds ratio; CI, confidence interval; NBC, nuclear, biologic, and chemical warfare; POW, prisoner of war.
† Controlled for gender, age, marital status, education, rank, and employment status on follow-up.

TABLE 5.   Association between reported exposures and multiple chemical sensitivity in Gulf veterans, British military personnel, 1997–1998

Multiple chemical sensitivity	Unadjusted OR*	95% CI*	Adjusted OR†	95% CI
Diesel or petrochemical fumes	1.8	0.7, 4.6	2.2	0.8, 5.9
NBC* suits	3.3	1.0, 10.6	2.8	0.8, 9.2
Pyridostigmine bromide	1.5	0.6, 3.5	1.6	0.6, 4.0
Exhaust from heaters	2.0	0.9, 4.8	2.8	1.1, 7.5
Smoke from oil fires	4.3	1.6, 12.2	4.6	1.6, 13.3
Hear chemical alarms	2.7	1.2, 6.5	2.5	1.0, 5.9
Personal pesticides	10.6	2.6, 43.9	10.9	2.6, 45.8
Local food	0.8	0.4, 1.6	0.9	0.5, 1.7
Burning rubbish/feces	5.8	2.1, 16.2	5.8	2.0, 16.7
Diesel on skin	1.7	0.9, 3.2	1.7	0.8, 3.6
Dismembered bodies	4.5	1.8, 11.4	4.2	1.6, 11.0
Other paints or solvents	2.2	1.1, 4.4	2.4	1.1, 5.1
Dead animals	2.4	1.2, 4.6	3.0	1.5, 6.1
POWs*	4.3	2.0, 9.3	4.0	1.8, 8.9
Maimed soldiers	3.8	1.9, 7.8	3.2	1.6, 6.5
Pesticides on clothing	11.3	4.8, 27.0	12.3	5.1, 30.0
Chemical/nerve gas attack	3.8	1.9, 7.6	3.2	1.5, 6.7
Mustard gas	4.2	1.4, 12.0	2.5	0.8, 7.9
Combat-related injury	3.4	1.6, 7.0	2.2	1.0, 4.9
Witness anyone dying	2.3	1.3, 4.1	2.2	1.2, 4.2
SCUD missile explosion	1.8	1.0, 3.4	1.6	0.8, 3.0
Small-arms fire	2.1	1.2, 3.7	2.1	1.1, 3.9
Artillery close by	2.8	1.5, 5.0	2.7	1.4, 5.0

* OR, odds ratio; CI, confidence interval; NBC, nuclear, biologic, and chemical warfare; POW, prisoner of war.
† Controlled for gender, age, marital status, education, rank, and employment status on follow-up.

TABLE 6. Odds ratios for health outcomes in chronic fatigue syndrome, British military personnel, 1997–1998

	No. with CFS* (% cases)	Unadjusted OR*	95% CI*	Adjusted OR†	95% CI
GHQ*	72 (93.1)	21.6	8.7, 53.8	20.7	6.4, 66.9
PTSR*	73 (50.7)	7.3	4.6, 1.7	4.5	2.6, 7.9

* CFS, chronic fatigue syndrome; OR, odds ratio; CI, confidence interval; GHQ, General Health Questionnaire; PTSR, postraumatic stress reaction.
† Controlled for gender, age, marital status, education, rank, and employment status on follow-up.

DISCUSSION

This paper reports the first operationally defined prevalence numbers for CFS (0.7–2.1 percent) and MCS (0.2–1.3 percent) in an epidemiologic survey of British military personnel. Gulf War veterans were at high risk of both disorders, although the prevalence of CFS in Gulf War veterans was greater than that in the Bosnia cohort but not in the Era cohort.

The limitations of a postal questionnaire survey in this population are discussed in detail in our earlier paper (3). All of the responses were questionnaire based and relied upon self-report, with case definitions being derived from them. The use of MCS as a diagnosis remains the subject of debate, and as such, there is no generally accepted case definition (7). Nevertheless, this presentation of multiple unexplained symptoms does merit investigation, and our use of operational criteria, while not conferring validity, allows group comparisons to be made. The small number of cases of CFS and, particularly, MCS increased the potential for type 2 errors; however, the strengths of this study include the high response rate, the use of two control groups, and the large population-based samples.

Very high levels of psychiatric comorbidity were demonstrated in both disorders. Given the results of previous work (19, 22), this is not surprising, although the near-universality of morbidity as measured by the General Health Questionnaire is a notable finding.

As one would expect, subjects with MCS were more likely to report exposures during their deployment than were other veterans. CFS was significantly associated with fewer exposures. The exposures reported cover a broad range—dead bodies, maimed soldiers, burning rubbish, etc.

TABLE 7. Odds ratios for health outcomes in multiple chemical sensitivity, British military personnel, 1997–1998

	No. with MCS* (% cases)	Unadjusted OR*	95% CI*	Adjusted OR†	95% CI
GHQ*	45 (95.6)	34.1	8.2, 141.0	24.4	5.8, 102.2
PTSR*	46 (73.9)	20.2	10.4, 39.2	14.6	7.2, 26.6

* MCS, multiple chemical sensitivity; OR, odds ratio; CI, confidence interval; GHQ, General Health Questionnaire; PTSR, postraumatic stress reaction.
† Controlled for gender, age, marital status, education, rank, and employment status on follow-up.

However, a striking finding was that of the strong association (12-fold increase in risk) between MCS and pesticides (in the form of creams, sprays, flea collars, or contaminated bedding and clothing). There was no similar association with CFS. Pesticide exposure is widely considered to be a precipitant of MCS, although conclusive evidence for this is lacking (7). The use of pesticides has also been implicated as a potential cause of chronic ill health in Gulf War veterans (23). The cross-sectional nature of this study, as well as the difficulties of verification of reported exposure, prevents conclusions from being drawn about causality. In addition, other chemical exposures—contact with diesel, paints, solvents, or toxic gases—did not show a similar degree of association. Theories about MCS would suggest that these should be similarly associated with symptoms, but media coverage in the United Kingdom has been largely confined to the pesticide question, suggesting that recall bias may be relevant, regardless of whether the subjects have given their symptoms the MCS label.

CFS and MCS have been investigated by questionnaire survey in previous studies of Gulf War veterans (1, 5, 24). In our systematic, epidemiologic study (3), 3.2 percent of Gulf War veterans believed or had been told that they had CFS, with 0.8 percent reporting MCS. The Iowa Persian Gulf Study Group (5) found that from 1 percent (regular military) to 2.9 percent (reservist) of Gulf War veterans reported symptoms of chronic fatigue as opposed to 0.2–1.1 percent in non-Gulf War veterans. Five percent of Gulf War veterans (2 percent of non-Gulf War veterans) reported symptoms of chemical sensitivity in the study by Fukuda et al. (1). They also interviewed a sample of the Gulf War veterans and, using the CDC criteria for CFS (17), estimated a prevalence of 5 percent. Kipen et al. (24) reported on 1,161 members of the Veteran Affairs' Gulf Registry who responded to a questionnaire survey. Sixteen percent of the veterans reported symptoms of CFS, as defined by the CDC, and 13 percent reported symptoms of MCS. That our study has found a considerably lower prevalence of both conditions may reflect the role of selection bias in the sample of Kipen et al. (24), with registry examination being voluntary. Although our prevalence number is lower than that reported by Fukuda et al. (1) in Gulf War veterans, it is higher than many of the estimates made in civilian population studies (25). CFS was predicted by lower educational attainment, nonofficer rank (indicators of socioeconomic status), and non-White ethnicity, findings that are supported by previous work (26). This adds to the evidence that the apparent excess of White middle classes reported from every specialist clinic to date is due to referral/selection bias and is not a true risk factor. An association with female gender is a consistent finding in CFS. The lack of association in this study may be explained by the small number of women in the sample. It has been suggested that CFS may be more common among health professionals, but we found no association with those whose primary duty was in the medical services. For MCS, there was an association with lower educational attainment and with military rank, although this did not reach statistical significance. The lack of association with sociodemographic characteristics corresponds to the population-based survey

by Kreutzer et al. (11). This contrasts with clinic-based studies that again report that above-average education and high socioeconomic status are hallmarks of this illness (27). Indeed, the peculiar socioeconomic distribution of MCS in specialist clinics, which is the reverse of that expected if MCS is an occupational disease, may again be a product of selection bias.

Overlap between the two conditions was less frequent than was observed by others (28). Even more striking was the marked discrepancy between self-defined report of suffering from either MCS or CFS and fulfilling operational criteria. As has been previously argued (29), operational definitions and self-reported diagnoses are two almost entirely different entities. This has implications for future epidemiologic studies in which diagnoses are made by self-report.

In conclusion, the results of this study indicate that symptoms attributed to CFS and MCS may account for some of the medically unexplained illnesses reported by British veterans after deployment to the Gulf. The prevalence of CFS in Gulf War veteran populations is higher than that in civilian population-based studies. However, the prevalence in the Era cohort is also relatively high. This raises the question that CFS may be associated with military service, although another explanation is that the increased prevalence is a result of the social class distribution in that population. Unlike CFS, MCS appears to be particularly associated with service in the Gulf. MCS has not previously been reported in a British population study, yet it appears that this pattern of symptoms is present although not attracting that particular label. The relation between MCS and pesticide exposure deserves further exploration, particularly in light of the controversy surrounding the etiology and status of this syndrome.

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