ORIGINAL INVESTIGATION

Multiple Chemical Sensitivity Syndrome

Symptom Prevalence and Risk Factors in a Military Population

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Objective: To assess the prevalence of and risk factors for self-reported symptoms suggestive of multiple chemical sensitivities/idiopathic environmental intolerance (MCS/IEI) in Persian Gulf War (PGW) veterans from Iowa and a comparison group of PGW-era military personnel.

Methods: A population-based sample of Iowa military personnel was surveyed using a cross-sectional telephone interview. Study participants were randomly drawn from 1 of 4 domains: PGW active duty, PGW National Guard/Reserve, non-PGW active duty, and non-PGW National Guard/Reserve. A complex sample survey design was used selecting participants from the following substrata: age, sex, race, rank, and military branch. The criteria for MCS/IEI were developed using expert consensus and the medical literature.

Results: A total of 3695 study participants (76% of those eligible) completed the telephone survey. The prevalence of symptoms suggestive of MCS/IEI in all participants was 3.4%. Veterans of the PGW reported a significantly higher prevalence of symptoms suggestive of MCS/IEI than did non-PGW military personnel (5.4% vs 2.6%); greater sensitivity to organic chemicals, vehicle exhaust, cosmetics, and smog; and more lifestyle changes. The following risk factors for MCS/IEI were identified with univariate analysis: deployment to the Persian Gulf, age (>25 years), female sex, receiving a physician diagnosis of MCS, previous professional psychiatric treatment, previous psychotropic medication use, current psychiatric illness, and a low level of preparedness. Multiple logistic regression analysis identified several independent risk factors for MCS/IEI, including deployment to the Persian Gulf, age, sex, rank, branch of service, previous professional psychiatric treatment, and current mental illness.

Conclusions: Self-reported symptoms suggestive of MCS/IEI are relatively frequent in a military population and are more common among PGW veterans than comparable controls. Reported chemical sensitivities and accompanying behavioral changes were also frequent. After adjusting for age, sex, and training preparedness, previous professional psychiatric treatment and previous psychotropic medication use (before deployment) showed a robust association with symptoms suggestive of MCS.

Arch Intern Med. 2000;160:1169-1176

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DEPLOYMENT during Operation Desert Storm has led to medical complaints from many veterans collectively referred to as the "Gulf War syndrome."[1,2] These varied symptoms range from relatively minor complaints (eg, skin rash and headache) to more profound problems, including neurologic and cognitive impairment.[3] Although the validity of the Gulf War syndrome is still being debated, it is clear that Persian Gulf War (PGW) veterans report more physical and psychologically based symptoms than do controls.[1] The Iowa Persian Gulf Study Group[4] recently reported the results of a large population-based telephone survey of Iowa PGW veterans and a comparison group of nondeployed military personnel from units activated and eligible for deployment during the same period. Veterans of the PGW reported significantly higher rates of a priori outcomes of symptoms suggestive of cognitive dysfunction, chronic fatigue, bronchitis, asthma, fibromyalgia, depression, posttraumatic stress disorder, alcohol abuse, anxiety, and sexual discomfort than did non-PGW era personnel.

An aberrant response to organic chemicals through airborne or other routes of exposure is one potential explanation for the symptoms reported by PGW veterans.[5,6] According to this hypothesis, exposure to oil and gas fumes or other chemical agents may be partly responsible for their complaints, which may represent a form of the multiple chemical sensitivity

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PARTICIPANTS AND METHODS

STUDY SAMPLE

The sampling design and survey methods are described in detail elsewhere.[4] Briefly, 4886 participants were randomly selected from 1 of 4 domains: PGW active duty, PGW National Guard/Reserve, non-PGW active duty, and non-PGW National Guard/Reserve. Military personnel were eligible for inclusion if Iowa was listed as the home of record on the individual's initial military record and the individual served in an active-duty or National Guard or US Reserve unit sometime between August 2, 1990, and July 31, 1991, which included Operation Desert Shield and Desert Storm (PGW period). The final sample was drawn from a potential study population of 28 968 persons. Active-duty personnel included those classified as serving at some time in the PGW period. National Guard/Reserve personnel included those classified as National Guard or US Reserve personnel sometime during the PGW period. Within each domain, the sample was further stratified by age, sex, race, rank, and branch of service. All individuals within very small strata (1-2 persons) were selected for participation.

ASSESSMENTS

A structured telephone interview was developed by the Iowa Persian Gulf Study Group[4] to assess a broad range of health concerns and to determine the self-reported prevalence of symptoms suggestive of specific conditions. Whenever possible, standardized questions, instruments, and scales were used to enhance the validity and generalizability of the results.

MCS/IEI OUTCOME DEFINITION

A panel of physician experts in allergy, immunology, occupational health, environmental health, clinical epidemiology, and psychiatry developed an operational definition for MCS/IEI based on a review of existing case definitions and our experience.[5] The criteria (**Table 1**) require that a person report illness from chemical sensitivity, report sensitivity to 2 or more types of incitants, have symptoms in at least 2 organ systems, and manifest evidence of impairment or behavioral change in response to the perceived sensitivity.

OTHER DEFINITIONS

Specific symptom patterns were defined a priori for suggestion of a particular disorder. Most were defined based on answers to multiple questions and using accepted criteria from standardized instruments and the medical literature. The PRIME-MD,[20] which is based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*,[21] was the source of questions and definitions of major depression, panic disorder, and generalized anxiety disorder. Major depression in the past month required 5 or more depressive symptoms. Minor depression was defined as feeling depressed or hopeless, or expressing little interest or pleasure in life, and having 2 to 4 additional depressive symptoms rated moderate to severe during the past month. Chronic dysphoria required depressive symptoms that caused impairment for 2 years or more. Chronic dysphoria corresponds to the *DSM-IV* diagnosis of dysthymia but does not fully overlap. Panic disorder required evidence of 1 or more spontaneous panic attacks during the past month accompanied by impairment. Generalized anxiety disorder required 3 or more symptoms of anxiety for the past year and anxiety or worry more days

(MCS) syndrome. Although MCS is not generally accepted by mainstream medicine,[7,8] and a Scientific Council of the American Medical Association[9] urged that it not be recognized, a growing body of literature[10-12] has documented that many persons in the United States and elsewhere have developed a similar set of symptoms that they and some physicians attribute to chemical exposures.

Proponents of the MCS syndrome[5,11-16] believe that the disorder is caused by extreme sensitivity to various chemical "incitants" in concentrations that are ordinarily well tolerated. Persons diagnosed with the MCS syndrome are polysymptomatic, report becoming ill when exposed to chemicals, and report that improvement is associated with avoidance of suspected incitants.[5] Common symptoms include weakness, fatigue, confusion and memory loss, depression, respiratory distress, gastrointestinal tract complaints, and migratory joint pains.[10-12] Many of these complaints are similar to those reported by PGW veterans.[1-3]

The medical community has remained largely skeptical, in part because the MCS syndrome has never been reliably linked with abnormal physical examination findings or laboratory values,[7-9] and recommended treatments have not been shown to be effective.[13-17] In fact, there are no convincing data that actual chemical sensitivity is the operative mechanism in MCS. Recently, the World Health Organization held a conference to consider MCS.[18] Although conceding that the validity of MCS has not been established, conferees urged that research continue to explore the phenomenon. They proposed the term "idiopathic environmental intolerance" (IEI) because many persons are thought to develop symptoms in response to environmental agents other than chemicals. For this reason, we will henceforth refer to these conditions as MCS/IEI.

Because MCS/IEI may potentially explain the symptoms of ill military personnel returning from the Persian Gulf, we sought to explore the association between MCS/IEI and PGW service in a population-based sample of Iowa military personnel. In this analysis, we assessed the prevalence of MCS/IEI and its symptoms in PGW veterans and nondeployed military personnel and its risk factors. Relatively little data have been reported on community prevalence of MCS/IEI so that another goal of this article is to assess its prevalence in a large population-based sample. We hypothesized that PGW veterans would report more symptoms of MCS/IEI than would nondeployed personnel and that persons with MCS/IEI would show a higher prevalence of predeployment psychiatric symptoms and disorders. Disability and functional im-

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than not during the past 6 months. Posttraumatic stress disorder was assessed based on a cutoff score of 50 or more from the Posttraumatic Stress Disorder Checklist.[22] Alcohol abuse was defined from items taken from the PRIME-MD and the CAGE questionnaire[23] and does not fully correspond to the *DSM-IV* criteria. Evidence of drinking during the past month and developing consequences as a result (eg, "a doctor told you to quit drinking") was required. Fibromyalgia required the participant to report being diagnosed as having fibromyalgia or fibrositis or having overall body pain for 3 months or more in the past year. The cognitive dysfunction assessment was based on questions from the Sickness Impact Profile,[24] the Chalder Fatigue Scale,[25] and investigator-derived items. Other medical outcomes assessed included chronic fatigue, respiratory symptoms (ie, acute and chronic airway disease), traumatic injuries, cancer, and sexual discomfort. Additional details about these a priori definitions can be found elsewhere.[4]

STUDY PROTOCOL AND DATA COLLECTION

The Statistical Laboratory Survey Section of the Department of Statistics at Iowa State University, Ames, conducted the telephone interviews. An initial interview was used to obtain the participant's consent, confirm the accuracy of the stratification data, and collect demographic information. Health assessments were conducted during the main telephone interview. The interviews were conducted between September 1995 and May 1996.

Direct supervision and monitoring continued during data collection. Interviewers attended a 4-day training session, which involved lessons and practice with computer-assisted telephone interviewing and its specific components and mock interviews. Ten percent of each interviewer's work was randomly selected and monitored, and interviewers received regular feedback and evaluation. Supervisory review of all interviews was performed before submission for coding and data processing. Test-retest reliability was moderate to excellent across medical and psychiatric variables tested in the nearly 5% of participants who completed the main interview and were reinterviewed 2 to 4 weeks later.[4]

DATA ANALYSIS

Prevalence rates of MCS/IEI and additional medical and psychiatric conditions were compared among each of the 4 study domains. Alpha was established at .05, and all *P* values were 2 tailed. Ninety-five percent confidence intervals were calculated for each estimate. The sampling design was a stratified random sample with oversampling in small cells. All statistical analyses were performed using SUDAAN[26] to account for the complex sample survey. Rates reported are based on the sampling design. For example, the study identified 169 participants who satisfied our criteria for MCS/IEI. Rates for this group are not the rates observed in this group of 169 individuals. They are weighted estimates based on weights dictated by the survey design.

All univariate rates, SEs, and odds ratios (ORs) were computed using the cross-tabulation procedure in SUDAAN. The ORs are unadjusted and do not account for differences in potential confounding variables. Logistic regression analysis was used to examine risk factors for MSC/IEI in the total study sample. These estimates are adjusted for age, sex, race, rank, branch, and military status. Stepwise regression techniques were used to identify independent risk factors for MCS/IEI. Because SUDAAN does not provide stepwise procedures, variable selection was performed in SAS statistical software.[27] A final model including those variables identified by SAS statistical software was run to obtain valid parameter estimates and their SEs.

pairment in persons with MCS/IEI are explored elsewhere.[19]

RESULTS

Table 2 shows the study sample characteristics. The sample included 4886 eligible participants who were proportionately distributed across the 4 study domains and 5 strata (age, sex, race, branch of service, and rank). Overall, 3695 (76%) of the eligible participants and 91% of those for whom a valid telephone number was identified completed the main telephone interview. Most participants were men, 25 years or younger, and married. Most participants were white, reflecting the general population of the state of Iowa, and had achieved a high school education or less. As expected, most military personnel were enlisted rather than officers. The Army was the most heavily represented branch of service, and the Air Force was the least represented.

The estimated population prevalence of symptoms suggestive of MCS/IEI are displayed in **Table 3**. A total of 169 participants overall (3.4%) met operational criteria for MCS/IEI. Overall, 2% reported having received a diagnosis of MCS/IEI from a physician. Among those who met criteria for MCS/IEI, more than one quarter (29%) had previously reported a physician diagnosis of MCS/IEI. Common sensitivities reported in this group included organic chemicals and solvents (83%); vehicle exhaust (69%); cosmetics (59%); pesticides, herbicides, and fertilizers (48%); and cigarette smoke (48%). Previous treatments reported included lifestyle change (83%); use of masks, gloves, or special clothes (43%); and use of special vitamins, supplements, or diets (28%).

Table 4 compares prevalence rates of MCS/IEI and its symptoms and treatment between deployed and nondeployed participants. Deployed military personnel were nearly twice as likely as the nondeployed to report symptoms suggestive of MCS/IEI (OR, 1.92); they were also more likely to report receiving a physician diagnosis of MCS/IEI and to report sensitivities to smog; cigarette fumes; vehicle exhaust; organic chemicals and solvents; and cosmetics, perfumes, or hair spray. The deployed were also significantly more likely than the nondeployed to report changing their lifestyle in response to chemical sensitivity.

Table 5 presents prevalence rates and ORs of medical and mental health conditions in military personnel with (n = 169) and without (n = 3526) symptoms suggestive of MCS/IEI. Participants meeting our MCS/IEI criteria were at increased risk for all the conditions listed

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Table 1. Criteria for MCS/IEI*

A. Routine or normal levels of exposure to chemical agents/substances (eg, gasoline, hair spray, paint, perfume, and soap) caused respondent to feel ill
B. Sensitivity (or illness after exposure) is reported to ≥2 of the following:
   1. Smog/air pollution
   2. Cigarette smoke
   3. Vehicle exhaust/fumes
   4. Copiers, printers, and office machines
   5. Newsprint
   6. Pesticides, herbicides, and fertilizers
   7. New buildings
   8. Carpeting and drapery
   9. Organic chemicals, solvents, glues, paints, and fuel
   10. Cosmetics, perfumes, hair spray, deodorants, and nail polish
   11. Other
C. Symptoms are reported from ≥2 of the following categories:
   1. Constitutional (eg, fever, night sweats, fatigue, weight loss, and weight gain)
   2. Rheumatologic (eg, joint pain and muscle aches)
   3. Neurologic (eg, headaches, sensory loss, tingling, and paralysis)
   4. Cardiovascular (eg, palpitations)
   5. Gastroenterologic (eg, gas, bloating, and abdominal pain)
   6. Dermatologic (eg, rash and blisters)
   7. Pulmonary (eg, shortness of breath, cough, and wheezing)
   8. Cognitive (eg, confusion, difficulty concentrating, and memory loss)
D. Symptoms lead to a behavioral change in ≥1 of the following ways:
   1. Wearing a mask, gloves, or special clothes
   2. Changing one's lifestyle to minimize chemical exposure
   3. Moving to a new home/location
   4. Use of special vitamins, supplements, or diets
   5. Use of oxygen, antifungal agents, or neutralizing injections/drops

*MCS/IEI indicates multiple chemical sensitivity/idiopathic environmental intolerance.

Table 2. Social, Demographic, and Military Characteristics in Deployed and Nondeployed Study Participants*

Characteristic	Military Status, % of Participants: Deployed (n = 1896)	Not Deployed (n = 1799)
Age, y		
≤25	60.0	52.0
>25	40.0	48.0
Sex		
Male	95.0	89.6
Female	5.0	10.4
Marital status		
Single/never married	20.3	17.2
Married	70.3	70.8
Separated/divorced/widowed	9.4	12.0
Education		
High school graduate or less	46.5	42.5
Some college	38.3	40.6
College graduate or beyond	14.1	16.9
Rank		
Enlisted	92.5	90.2
Officer	7.5	9.8
Branch		
Army	50.8	35.5
Air Force	9.6	28.5
Marines	18.7	9.4
Navy/Coast Guard	20.9	26.6
Race		
White	95.8	96.7
Black or other	4.2	3.3

*Rates are generated by SUDAAN[26] to account for the complex sampling design. They are not adjusted for covariates.

except alcohol abuse and cancer. For example, military personnel with symptoms suggestive of MCS/IEI had more than 10 times the odds of reporting symptoms of major depression than did personnel without symptoms (OR, 10.4). In the total sample with symptoms suggestive of MCS/IEI, both medical and psychiatric health conditions were highly prevalent, particularly symptoms of respiratory conditions (76%), fibromyalgia (59%), "any" depression (56%), cognitive dysfunction (55%), minor depression (52%), and traumatic injuries (38%).

Table 6 displays the results of univariate logistic regression analysis comparing potential risk factors between those who satisfied our criteria for MCS/IEI with those who did not. These ORs are adjusted for age, sex, race, branch of military, and rank. Significant risk factors included female sex; age greater than 25 years; low level of preparedness (rated on a 1-6 scale, with 1 indicating less prepared and 6, more prepared); a physician diagnosis of MCS/IEI; previous professional psychiatric treatment; previous psychotropic medication use (before August 1990); current symptoms suggestive of "any" depression, posttraumatic stress disorder, generalized anxiety disorder, or panic disorder; and deployment to the Persian Gulf.

Multivariate logistic regression analysis suggested several independent risk factors for MCS/IEI. After adjusting for other risk factors, the odds that a participant who was deployed to the Gulf would satisfy our criteria for MSC/IEI was 1.94 (95% confidence interval, 1.16-3.24). Other risk variables significant at the 5% level or less included age, sex, rank, and branch of service. Psychiatric risk factors included previous professional psychiatric treatment (OR, 2.31) and the presence of current "any" depression (OR, 4.87), panic disorder (OR, 2.27), or generalized anxiety disorder (OR, 2.22).

COMMENT

These results demonstrate the utility of our operational definition for MCS/IEI. Because standardized criteria for MCS/IEI were unavailable when this study was organized, we developed our own after we reviewed several definitions, including that of Cullen,[28] which emphasizes the development of symptoms in response to chemical exposure. Our criteria join others that have recently been proposed and seem to distinguish persons with complaints typical of MCS/IEI from others.[29,30] Although epidemiological studies of this condition are just getting under way, the finding that 2.5% to 3.0% of nondeployed military personnel meet our criteria for MCS/IEI is similar to the rate of 4.0% of individuals surveyed by Kreutzer et al,[30] who claimed to be sensitive to "a lot of different chemicals." Meggs et al[11] had earlier reported that 3.9% of respondents to a North Carolina telephone survey ex-

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Table 3. Estimated Population Prevalence Rates of MCS/IEI, Its Symptoms and Treatment in All Participants, and Those Who Meet Study Criteria for MCS/IEI*

	Estimated Prevalence Rate (SE)	
	All Participants (N = 3695)	Participants Who Meet Criteria for MCS/IEI (n = 169)
Meets study criteria for MCS/IEI	3.35 (0.37)	100.00
Physician-diagnosed MCS/IEI	2.21 (0.31)	28.64 (5.55)
Reports chemical sensitivity	7.99 (0.56)	100.00
Reported sensitivity to		
Smog	1.40 (0.22)	28.84 (4.86)
Cigarette smoke	2.73 (0.34)	47.66 (5.62)
Vehicle exhaust	3.29 (0.35)	69.37 (5.43)
Copiers, printers, and office machines	0.22 (0.09)	4.71 (2.46)
Newsprint	0.24 (0.12)	6.80 (3.42)
Pesticides, herbicides, and fertilizers	1.90 (0.29)	48.44 (5.74)
New buildings	0.53 (0.13)	14.80 (3.62)
Carpeting and drapery	0.32 (0.11)	9.57 (3.18)
Organic chemicals, solvents, glues, paint, and fuel	4.54 (0.44)	82.56 (4.40)
Cosmetics, perfumes, and hair spray	3.16 (0.37)	58.77 (5.44)
Reported treatment		
Mask, gloves, and special clothes	2.42 (0.32)	42.57 (5.53)
Changed lifestyle	5.23 (0.46)	82.53 (4.48)
Moved to new home/location	1.56 (0.26)	25.09 (4.55)
Vitamins, supplements, and diet	1.60 (0.28)	27.84 (5.24)
Oxygen, antifungals, and neutralizing agents	0.73 (0.19)	16.10 (4.33)

**MCS/IEI indicates multiple chemical sensitivity/idiopathic environmental intolerance. Rates are generated by SUDAAN[26] to account for the complex sampling design. They are not adjusted for covariates.*

Table 4. Estimated Population Prevalence Rates of MCS/IEI, Its Symptoms and Treatment, and Odds Ratios Comparing Rates in Deployed With Rates in Nondeployed Military Personnel*

	Estimated Prevalence Rate (SE)		
	Deployed (n = 1896)	Not Deployed (n = 1799)	Odds Ratio (95% CI)
Meets study criteria for MCS/IEI	5.41 (0.55)	2.55 (0.47)	1.92 (1.22-3.04)
Physician-diagnosed MCS/IEI	3.59 (0.48)	1.68 (0.39)	2.00 (1.35-3.52)
Reports chemical sensitivity	12.82 (0.83)	6.12 (0.70)	1.94 (1.45-2.60)
Reported sensitivity to			
Smog	2.83 (0.41)	0.85 (0.26)	3.39 (1.67-6.86)
Cigarette smoke	4.39 (0.52)	2.09 (0.42)	1.86 (1.14-3.03)
Vehicle exhaust	5.63 (0.57)	2.39 (0.44)	2.10 (1.34-3.30)
Copiers, printers, and office machines	0.53 (0.20)	0.10 (0.10)	. . .
Newsprint	0.38 (0.13)	0.18 (0.16)	1.38 (0.37-5.11)
Pesticides, herbicides, and fertilizers	2.94 (0.43)	1.49 (0.37)	1.73 (0.94-3.21)
New buildings	0.90 (0.20)	0.38 (0.16)	1.83 (0.70-4.76)
Carpeting and drapery	0.46 (0.13)	0.27 (0.15)	. . .
Organic chemicals, solvents, glues, paint, and fuel	7.32 (0.64)	3.47 (0.55)	1.80 (1.21-2.68)
Cosmetics, perfumes, and hair spray	4.65 (0.52)	2.58 (0.47)	1.63 (1.05-2.53)
Reported treatment			
Mask, gloves, and special clothes	3.31 (0.44)	2.07 (0.41)	1.34 (0.80-2.26)
Changed lifestyle	8.25 (0.68)	4.06 (0.59)	1.76 (1.23-2.53)
Moved to new home/location	2.26 (0.39)	1.28 (0.33)	1.50 (0.80-2.82)
Vitamins, supplements, and diet	1.95 (0.34)	1.47 (0.37)	1.20 (0.62-2.36)
Oxygen, antifungal agents, and neutralizing agents	0.80 (0.21)	0.70 (0.25)	1.11 (0.45-2.72)

**MCS/IEI indicates multiple chemical sensitivity/idiopathic environmental intolerance; CI, confidence interval; and ellipses, too few data to calculate. Rates are generated by SUDAAN[26] to account for the complex sampling design. They are not adjusted for covariates. Odds ratios are adjusted for age, sex, race, branch of military, and rank and indicate the risk for an outcome for those meeting criteria for MCS/IEI compared with those not meeting criteria.*

perienced daily symptoms of chemical sensitivity, defined as becoming sick after smelling chemical odors.

As hypothesized, PGW veterans were almost twice as likely as non-PGW military personnel to report symptoms suggestive of MCS/IEI. Furthermore, persons with symptoms suggestive of MCS/IEI have a higher prevalence of current psychiatric symptoms and disorders. The latter finding is consistent with those of controlled and uncontrolled clinical studies[10,12,31-34] that show that persons diagnosed with MCS/IEI frequently meet criteria for mood disorders, anxiety disorders, and somatization disorder. Proponents of MCS/IEI argue that psychiatric disorders are a result of the disorder and not a risk factor or represent misclassification. They note that chronic, debilitating illnesses can lead to depression, anxiety, or unexplained physical complaints and that these same complaints could be induced by the biological processes underlying MCS/IEI.[15] Yet, these arguments do not explain why participants with MCS/IEI often have psychiatric comorbidity that predates presumed chemical exposures and the subsequent development of MCS/IEI.[10,31] Although this cross-sectional study was not designed to assess premorbid psychiatric comorbidity, participants were nonetheless asked about previous professional psychiatric treatment and previous psychotropic medication use (before August 1990). Both variables showed a robust association with symptoms suggestive of MCS/IEI.

The high prevalence of anxiety disorders—especially panic disorder—merits comment. Persons with MCS/IEI frequently report "chemical reactions" in response to strong odors,[5] the symptoms of which are nearly indistinguishable from panic attacks. Bolla-Wilson et al[35] proposed that MCS/IEI results from a behaviorally conditioned response to odors: a strong-smelling chemical irritant causes a direct and nonconditioned physical or psychophysiologic response. Later, exposure to the same odor at a much lower concentration may cause a conditioned response of the same symptoms. Through stimulus generalization, different odors or "incitants" could cause similar symptoms, which are

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Table 5. Estimated Prevalence Rates of Health Conditions and Odds Ratios Comparing Rates in Participants Who Meet Criteria for MCS/IEI With Those Who Do Not*

Current Condition	Estimated Prevalence Rate (SE)		Odds Ratio (95% CI)
	Meets Criteria for MCS/IEI (n = 169)	Does Not Meet Criteria for MCS/IEI (n = 3526)	
Major depression	33.84 (5.05)	4.25 (0.42)	10.40 (6.35-17.03)
Minor depression	52.35 (5.61)	10.18 (0.67)	8.28 (5.21-13.18)
Chronic dysphoria	19.99 (3.85)	3.47 (0.40)	5.70 (3.41-9.53)
Any depression	56.01 (5.60)	11.13 (0.70)	8.65 (5.42-13.79)
Generalized anxiety disorder	18.99 (4.32)	1.82 (0.28)	11.21 (5.76-21.83)
Panic disorder	15.05 (4.02)	1.28 (0.23)	11.06 (4.99-24.55)
Symptoms of fibromyalgia	59.17 (5.52)	10.66 (0.64)	10.30 (6.41-16.54)
Symptoms of chronic fatigue	6.11 (2.23)	0.39 (0.10)	12.50 (3.54-44.10)
Symptoms of PTSD	9.57 (3.14)	0.79 (0.18)	9.91 (4.06-24.16)
Symptoms of cognitive dysfunction	55.31 (5.63)	9.18 (0.59)	10.18 (6.44-16.10)
Respiratory symptoms	76.43 (4.63)	23.48 (0.94)	9.26 (5.56-15.42)
Alcohol abuse	16.54 (4.06)	13.85 (0.75)	1.28 (0.70-2.34)
Reported injuries	38.46 (5.43)	22.97 (0.95)	2.27 (1.44-3.59)
Any cancer	2.05 (0.93)	0.98 (0.22)	2.30 (0.79-6.69)
Sexual discomfort	4.94 (2.19)	1.05 (0.22)	3.96 (1.36-11.56)

**MCS/IEI indicates multiple chemical sensitivity/idiopathic environmental intolerance; CI, confidence interval; and PTSD, posttraumatic stress disorder. Rates are generated by SUDAAN[26] to account for the complex sampling design. They are not adusted for covariates. Odds ratios are adjusted for age, sex, race, branch of military, and rank and indicate the risk for an outcome in those meeting criteria for MCS/IEI compared with those not meeting criteria.*

Table 6. Univariate Logistic Regression Analysis of Risk Factors for MCS/IEI in the Total Population*

	Wald Test	P	Odds Ratio† (95% CI)
Deployment status			
Persian Gulf War deployment (no)	7.71	.006	1.92 (1.22-3.04)
Sociodemographic and personality characteristics			
Age (<25 y)	4.84	.03	1.69 (1.06-2.68)
Sex (male)	6.96	.008	2.58 (1.28-5.19)
Marital status (single)	0.89	.41	. . . (Reference)
Married	1.60	.21	1.49 (0.81-2.76)
Separated/widowed/divorced	0.17	.68	1.18 (0.55-2.54)
Spent time in jail (no)	2.87	.09	1.51 (0.94-2.42)
Education (<high school)	1.46	.23	. . . (Reference)
Some college	2.61	.11	1.52 (0.92-2.51)
College degree or more	1.23	.27	1.57 (0.71-3.49)
Physician-diagnosed MCS/IEI (no)	113.45	<.001	27.76 (15.12-50.95)
Smoking (never)	0.31	.73	. . . (Reference)
Former	0.47	.49	1.23 (0.68-2.20)
Current	0.42	.52	1.20 (0.70-2.04)
Court martialed (no)	0.70	.40	2.00 (0.40-9.99)
Military discipline (no)	2.74	.10	1.55 (0.93-2.60)
Marlow-Crowne Social Desirability Scale (0-10)	3.82	.05	0.90 (0.81-1.00)
Sometimes get even rather than forgive/forget (no)	1.75	.19	1.35 (0.87-2.10)
Occasionally have felt like smashing things (no)	3.48	.06	1.64 (0.98-2.75)
Level of preparedness (1-6)‡	10.04	.002	0.59 (0.42-0.82)
Psychiatric history			
Ever seen a professional for mental health (no)	33.57	<.001	4.03 (2.52-6.43)
History of any of the following before August 1990			
Illegal or street drug use (no)	0.01	.92	0.98 (0.61-1.56)
Prescribed psychiatric medication (no)	3.98	.05	3.12 (1.03-9.46)
Psychiatric hospitalization (no)	0.23	.63	1.48 (0.30-7.45)
Attempted suicide	0.28	.60	1.49 (0.34-6.53)
Jail time (no)	1.69	.19	1.43 (0.84-2.45)
Current psychiatric conditions (symptoms suggestive of)			
Any depression (no)	83.07	<.001	8.70 (5.48-13.82)
Posttraumatic stress disorder (no)	26.53	<.001	10.26 (4.26-24.75)
Generalized anxiety disorder (no)	50.45	<.001	11.36 (5.48-22.10)
Panic disorder (no)	34.88	<.001	11.23 (5.06-24.93)

**MCS/IEI indicates multiple chemical sensitivity/idiopathic environmental intolerance; CI, confidence interval.*

†All values are adjusted for age, sex, race, rank, branch of military and indicate the risk for an outcome in those meeting criteria for MCS/IEI compared with those not meeting criteria.

‡Level of preparedness was self-assessed based on the sum of responses to 6 questions, with greater values reflecting complete preparedness.

experienced as "chemical reactions." Although this theory has not been experimentally verified, clinical experience suggests that this mechanism is likely operative in many persons reporting MCS/IEI, prompting Terr[36] to call them "chemophobic." The similarity of patient-reported "chemical reactions" to panic attacks led Leznoff[37] and Binkley and Kutcher[38] to use provocative challenges to assess the possible connection between MCS/IEI and anxiety. Leznoff[37] exposed 15 individuals to their self-reported chemical "trigger" substances, which induced hyperventilation in 73% and produced a rapid decrease in partial pressure of carbon dioxide. Binkley and Kutcher[38] administered intravenous sodium lactate to 5 patients with MCS/IEI, inducing a panic attack in each. Both studies suggest that anxiety is a causal mechanism in at least some cases of MCS/IEI. For many, it seems that they have developed "odor-triggered" panic attacks.[39]

No personality instruments were included in our assessment, although several questions that tap antisocial traits were examined for their relationship to MCS/IEI. None of these items proved to have an important association with MCS/IEI. Results of clinical research[40,41] suggest that although many persons diagnosed with MCS/IEI have abnormal personality traits, they are not at risk for antisocial personality disorder. Participants with MCS/IEI were not at risk for alcohol abuse either, another finding consistent with clinical study results.[10,12,31]

How do we explain the findings? One potential explanation is that military personnel deployed to the Persian Gulf were exposed to chemical agents that induced

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MCS/IEI. The fact that nondeployed military personnel also reported symptoms of MCS/IEI shows that the symptoms are not unique, although they occurred at a higher rate in deployed PGW veterans. Our findings are consistent with those of Fukuda et al,[42] who found that 5% of Air National Guard personnel in a single unit deployed to the Persian Gulf reported "chemical sensitivity" compared with 2% of nondeployed Air Force personnel. Furthermore, the results do not explain why deployed National Guard/Reserve personnel were at greater risk for symptoms suggestive of MCS/IEI than were active-duty military personnel. In fact, National Guard/Reserve personnel spent less time in the PGW theater, were more likely to be involved in combat support roles, and probably had fewer environmental exposures than did active-duty personnel. However, the National Guard/Reserve personnel were older, were more educated, and may have been less well prepared for combat.[4] Because they were not on active duty and were called to PGW service, their experience may have been more physically demanding and psychologically disruptive. Because stress is well known to induce physical and emotional symptoms of illness in some persons, perhaps the increased prevalence of MCS/IEI in National Guard/Reserve personnel reflects the stressful nature of their service in this conflict.

Another potential explanation is differential recall. Recall bias is a poorly understood but well-recognized problem in retrospective studies and can substantially alter the frequency of symptom reports.[43] Media reports and, perhaps, health care professionals may have unwittingly led PGW veterans to become overly concerned about the possibility of developing chemical sensitivity or other unexplained illnesses and to report more symptoms. Veterans of the PGW with emotional disorders, or those having sought treatment for one, may simply be more vulnerable to the process of suggestion. Thus, recall bias may be responsible for artificially inflating the number and frequency of reports of chemical sensitivity and both psychiatric and functional somatic symptoms as well. Because a significant risk factor for reporting symptoms suggestive of MCS/IEI is a physician diagnosis of the same, it may be that iatrogenic reinforcement plays a role in accepting the diagnosis and in maintaining illness belief.[44]

There are several methodological limitations to the study. First, restricting the study to veterans originally from Iowa may limit the generalizability of the data. Iowa has relatively few minority members, and some persons may have had unique exposures related to agriculture. Second, differential participation by selected demographic subgroups may further limit the ability to generalize these results to other populations, although participation rates were high in all branches. In any event, deployed participants in this study were distributed throughout the Persian Gulf, suggesting that the military experiences of the deployed group probably can be generalized to other PGW veterans.[4] Third, the study depended on self-reported symptoms and exposures that were not independently verified because physical examinations and laboratory testing to rule out other disorders were not done and external sources of exposure data were not available. Also, although our questionnaire consists of standardized instruments, they were modified for telephone administration by lay interviewers, which could affect the validity of the results (eg, the PRIME-MD is designed for use by clinicians). Fourth, our definition of MCS/IEI was empirically derived by consensus of a group of experts. The definition has not been specifically tested for reliability or for evidence of validity in other settings. Finally, the analysis required multiple comparisons that could have revealed statistically significant relationships by chance alone. Because the study was designed to provide an overall description of MCS/IEI symptoms, we chose not to control for the number of comparisons. Selection of a more strict α level would have had little effect on these results.

Although our study findings show that complaints of chemical sensitivity are not rare, they provide no information on their clinical significance in terms of actual sensitivity and severity and do not explain why only 29% of MCS/IEI cases were so diagnosed by a physician. It may be that some persons meeting our criteria for MCS/IEI misinterpreted the questions or experienced mild or trivial reactions to exposures ranging from cigarette smoke to perfume that they or their physician thought unimportant. More extreme cases probably represent a much smaller fraction of those identified with the condition. The findings should not be interpreted as validating the concept of MCS/IEI as a unique disorder. The symptoms of MCS/IEI overlap with those of many other conditions, and additional work is necessary to determine whether it can be confirmed as a valid diagnosis. As noted previously, MCS/IEI has not been correlated with abnormal physical examination findings or laboratory values,[7-9] and participants' reports of chemical sensitivities have not been scientifically verified. For these reasons, many physicians may view MCS/IEI with skepticism and resist making a diagnosis that violates recommendations promulgated by the American Medical Association.

Nonetheless, the results show that many persons report chemical sensitivity, and their complaints cannot be ignored. This study, and the use of an operational definition for MCS/IEI, may help identify a group of persons requiring further study. Future investigations should focus on validating the reports of chemical sensitivity and, if confirmed, assess potential etiologic factors, including environmental contaminants, infectious agents, medications and vaccines, and psychological stressors.

Accepted for publication August 16, 1999.

This study was partially supported by a cooperative agreement with the Iowa Department of Public Health and The University of Iowa, Iowa City; grant U50/CCU711513 from the National Centers for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Ga; and grant DAMD 17-97-1 from the Department of Defense.

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