CME Article #2

Reported Exposures, Stressors, and Life Events Among Gulf War Registry Veterans

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Learning Objectives

- Summarize the prevalence and nature of symptoms in this survey of Gulf War veterans and the ways in which those with a high level of symptoms differ from their less symptomatic peers.
- Correlate symptom levels with war-related stressors, reported exposures, and adverse life events.
- Discuss relationships among reported exposure to chemical/biologic weapons, evidence of actual exposure, and unexplained symptoms in Gulf War veterans.

Abstract

We investigated the association of 15 exposures, 10 stressors, and 18 life events with illness symptoms reported by 978 veterans who believe they suffer from Gulf War-related illnesses. A mail survey was completed by veterans (60% response rate) from the Gulf War Health Registry. Variables most associated with high symptom group membership were reported chemical/biologic warfare (CBW), concerns with infection and faulty equipment, feelings of mistrust in the military, and disability leading to work stoppage within 2 years after the war. These data suggest that belief in CBW exposure, and the experience of war stress and serious negative life events after the war, are important concomitants of Gulf War illness. Models seeking to explain Gulf War symptoms need to incorporate a range of exposure and psychosocial factors to fully account for important influences. (J Occup Environ Med. *2003;45: 1247–1256*)

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The Gulf War saw nearly 697,000 American service personnel deployed to the Persian Gulf from 1990 to 1991. There were remarkably few combat casualties in the theater. However, shortly after their return to the United States, some veterans began reporting persistent, medically unexplained health problems potentially associated with environmental exposures. These health problems became broadly known as Gulf War illness and are best characterized as symptoms without explanatory underlying medical findings.[1] Although there has been controversy over whether Gulf War illness is a new condition, unexplained symptoms have been documented in both American[2] and British[3] troops after all modern wars, suggesting it is a recurrent issue.

It is well established that Gulf War-deployed veterans report subjectively worse health overall and more symptoms than their nondeployed peers,[4–7] although there is lack of agreement on the etiology of the increased symptoms. Prominent types of explored etiologies for Gulf War symptoms are environmental exposures,[4,7–9] prophylactic medical treatments,[4,7,10,11] and war stress.[9,12,13] Regardless of cause, veterans having substantial symptoms after serving in the Persian Gulf are worse off in terms of adverse life events after the war.[14]

In response to widespread concern about the issue, the Department of Veterans Affairs developed a registry in 1992 in which veterans with health complaints or concerns about future health were entered into a

database.[15] To date, more than 70,000 veterans have entered the registry. Not all the veterans in the registry believe themselves to be currently ill as the result of Gulf War service. However, the registry represents the largest group of veterans who believe they could have a Gulf War illness. If a Gulf War illness does exist, and people's self-reports are a good indicator for it, then this registry should be a rich source of cases, and the present study was designed to take advantage of this.

In the absence of demonstrable and cogent clinical findings to explain illness, Hallman et al.[16] used self-reported symptoms of a random sample of registry veterans to create a statistically derived case definition of Gulf War illness, in effect allowing the illness characteristics of the veterans themselves to define the illness without other criteria shaping the definition. Many other Gulf War studies are based on classifying veterans with respect to deployment status, a surrogate for many types of exposures and stressors, or have created case definitions. However, few have categorized an illness as defined purely by the veterans' self-report of symptoms. Doing so allows an intensive look at the relationship between exposure reports and self-reported symptoms within a deployed group.

The present study is an analysis of additional responses collected by Hallman et al.[16] investigating whether self-reported exposures, stressors, and life events occurred at different rates for case versus non-case registry veterans. Understanding those things associated with this manifestation of medically unexplained symptoms could facilitate treatment and prevention of future war-related illnesses.

Methods

Participants

Questionnaires were mailed to 2011 American Persian Gulf War veterans selected in a simple random procedure by the Veterans Administration's (VA) Environmental Epidemiology Service. Veterans were selected from the Gulf War Registry rolls of 7 states: Delaware, Illinois, New Jersey, New York, North Carolina, Ohio, and Pennsylvania. These states were chosen to facilitate the recruitment of participants for a separate follow-up study that included medical examinations at the VA Medical Center in East Orange, NJ. Individuals targeted for other major concurrent studies were excluded. To test for potential selection biases, available demographic data were obtained from the Registry for each veteran who received a questionnaire. These were compared with summary data from the entire Registry. Chi-squared analyses revealed no significant differences in the distribution of branch of service, duty status, or gender between those randomly selected to be in the sample and those in the registry as a whole.

The respondents were asked to examine a list of 48 symptom complaints. For each symptom, the respondents indicated whether they had experienced "persistent or recurring" problems within the last year, and if so, whether the problems they had experienced were "mild," "moderate," or "severe." Hallman et al.[16] used factor analysis to collapse the 48 symptoms into 4 main dimensions (mood, muscle, gastrointestinal, and throat/breathing), and then used cluster analysis to divide respondents into 2 groups according to these 4 main dimensions. These same 2 groups of veterans are the focus of the current study. One group of veterans endorsed a mean of 37 symptoms. These symptoms consisted of moderate/severe mood and muscle complaints, and mild/moderate gastrointestinal and throat/breathing complaints. This group will be referred to in the present study as the high-symptom group ($n = 387$). The remaining veterans endorsed a mean of 18 mild complaints and will be referred to here as the low-symptom group ($n = 591$).

Procedures

Mail procedures included an introductory letter, an initial questionnaire, followed by reminder postcards, a second identical letter and a questionnaire, and a maximum of 3 follow-up phone calls at approximately 2-week intervals until a response was received.

Materials

The respondents were asked 50 war experience questions regarding how much they believed they were exposed to a wide range of environmental hazards during their deployment such as blowing sands, oil-fire smoke, and chemical warfare. The 7-point response scale for these items ranged from "not at all" to "extremely" with "moderately" as the midpoint. Other items reflected whether the respondents had experienced other stressors while deployed such as firing at enemy troops, not getting enough to eat, or ruminative thoughts such as worrying about what might happen to them. These items also had a 7-point response scale, ranging from "never" to "always" with "sometimes" as the midpoint. These reported war experience items were factor-analyzed and combined to create composite scales.

The respondents also completed items about whether they had been wounded during the war or had witnessed a traumatic event. Respondents who endorsed the latter item completed the Impact of Events Scale[17] measuring symptoms of posttraumatic stress disorder (PTSD) over the week before filling out the questionnaire.

They also reported the number of days they wore a "gas mask" for any length of time and the number of days they wore 1 for at least 4 hours. This provides a proxy of exposure to the most stressful gas alarm incidents.

In addition, the respondents were asked about prophylactic immunizations they received and prophylactic oral medications they had taken, spe-

cifically, anthrax vaccine (injection), typhoid vaccine (injection), botulism vaccine (injection), immune globulin (IG gamma globulin), plague vaccine, meningococcus vaccine, malaria pills, and ciprofloxacin (anti-anthrax pill). The sum of these was also calculated for each respondent. Information was also collected about pyridostigmine bromide (PB) pill (antinerve gas pills) use. Respondents reported the number of days they took at least 1 pill and the number of days they took more than the recommended 3 pills.

Finally, the respondents were asked to indicate the occurrence of 18 important life events during 5 time periods: before 2 years before leaving for the Gulf, in the 2 years before leaving for the Gulf, during activation/deployment while serving in the Gulf, within 2 years of returning from the Gulf, and more than 2 years after returning from the Gulf. Some examples of life events assessed are divorce, employment disability, and bankruptcy.

Statistical Analyses

Factor Analysis and Scale Construction. Factor analysis is a statistical technique commonly used to "summarize the interrelationships among. . . variables in a concise but accurate manner as an aid in conceptualization."[18] In the present study, the 50 war experience items were factor analyzed using exploratory factor analyses. We used the principal axis method of extraction, which reproduces only the significant variance of the items and assumes much of the leftover variance is measurement error.[18]

An important factor analysis decision is how many factors to retain; extracting too few or too many can result in factors that include considerable error.[19] Published criteria were used to determine number of factors to retain.[20–22] The factors were rotated to Varimax to identify those items most closely associated with each factor. Scales were then constructed by summing the raw scores of the items with the greatest correlations with that particular factor. Internal consistency (Cronbach's alpha), was calculated for each scale. The scales were transformed by dividing by the number of items included in the scale to place the scores back in the original range of 1 to 7. The scales were then used as stressor or exposure variables.

Statistical Control. Although using a Registry sample is useful because of its intended accumulation of sicker individuals, it is problematic in that demographic groups that tend to have poorer health could be overrepresented. Efforts were made to statistically correct for a range of potentially confounding variables. These variables were race, age, gender, education, military branch, military rank, military duty, marital status at deployment, as well as self-reported health at deployment, alcohol use, smoking, illicit drug use, and PTSD symptoms. PTSD's potential effect on symptom reporting was assessed using the 10-item Impact of Events scale.[17] Only respondents who had endorsed experiencing a traumatic event filled out these items, so a scale was adapted to allow the inclusion of those who had not experienced a traumatic event. The Impact of Events scale uses a 5-point ordinal response scale. The mean response to all items was calculated and rounded to the nearest whole number. If a respondent had not experienced a traumatic event, they were put at the lowest number of the 5-point scale, representing no PTSD symptoms.

For all analyses, we examined the semipartial correlation between symptom group membership and the variable of interest after controlling for these potentially confounding variables.

Analyses of Symptom Group Differences. Hallman et al.'s[16] high and low symptom groups were compared on exposure or stressor variables. With a continuous stressor or exposure variable, we used hierarchical linear model analyses, a special case of the unified linear model method outlined by Cohen and Cohen.[23] With a nominal stressor or exposure variable, the Pillai-Bartlett trace[24] was used for significance tests. It uses a chi-square calculation instead of mean squares with an F ratio; however, the resulting P is interpreted the same.[25] In these analyses, the exposure or stressor variable was entered after the set of control variables.

Effect sizes were calculated to compare the relative sizes of the associations between symptom group membership and the various exposure and stressor variables, regardless of the level of variable measurement. For continuous variables, the effect sizes were calculated using semipartial multiple correlations (R), and for nominal variables, using semipartial eta. Both can be interpreted on Cohen's[26] qualitative scale of "small," 0.1; "medium," 0.3; and "large," 0.5.

We examined whether the symptom groups differed in their reports of major life events over time. The life events were analyzed to examine both group differences and whether the 2 groups changed at different rates. The group differences were analyzed by summing the instances of endorsed events over the 5 periods. For the rate of change analyses, change variables were calculated summarizing the difference between the endorsed life events at time 2 minus time 1, time 3 minus time 2, and so on, creating four variables. The group and rate of change variables were analyzed in a hierarchical linear model.

Missing Data and Outliers. There were no missing data for the symptom group membership variable or for the 18 life events variables. Cases with missing data for any of the exposure or stressor variables were not included in that particular analysis.

A handful of cases had missing control variable data. This was handled in nominal variables by adding a "missing" category. Continuous

variables with missing data, ranging from 6 to 16 cases in the full dataset, were handled in the manner recommended by Gorsuch.[21] The prophylactic treatment questionnaire items offered respondents 3 choices: "yes," "no," or "don't know." Respondents endorsing "don't know" on an item were not included in that particular analysis.

The gas mask variables had some substantial outliers. These were treated in a procedure recommended by Jedd and McClelland.[27]

Cumulative Type I Error Correction. With so many separate analyses, finding an analysis significant by chance was a concern. We used 2 strategies to correct for this. For analyses of the life events measures, we used Fisher's protected F test[28] recommended by Cohen and Cohen[23] to test for overall differences. As an initial step, the sets of group and rate of change effects for all 18 events were tested for significance, $P \leq 0.05$. Significance for both would give us license to then examine the effects of the particular life events. If a particular life event had overall significance for both group and rate of change differences, this event was further examined at each of the 5 periods.

Because of missing exposure and stressor variable data, each of the exposure and stressor analyses had a different N, making Fisher's protected F test impractical. Instead, following suggestions from Keppel,[29] we set the probability significance level for these analyses at $<.01$.

Results

Responses

Of the 2011 mailed questionnaires, 1935 were delivered, and 1161 were completed and returned by the respondents, a response rate of 60.0%. In the parent study,[16] no significant response biases were found for gender, date of entry into the registry, branch of service, type of unit, grade, specific symptoms, or specific diagnoses.

Of the 1161 respondents, 978 (84.2%) reported believing they have had medical problems as the result of their service in the Gulf War and had enough data to be classified according to the parent study.[16] Because the goal of this study is uncover elements of the veterans' experience associated with a self-reported Gulf War illness, only these 978 were included in further analyses.

Control Variables

The descriptive statistics of the demographic, health, substance abuse, and PTSD symptom control variables are shown in Table 1. Effect sizes with the symptom group variable are also shown. For nominal variables, odds ratios are also shown. The most notable differences were that those in the high-symptom group had more current PTSD symptoms, were less likely to be white, were less educated, were more likely to be separated from their spouse or living with a mate, smoked more cigarettes, and drank more alcohol.

Factor Analysis and Scale Construction

We extracted 10 factors, which accounted for 55% of the variance among all 50 items. Scales were constructed using the items indicated in Table 2. The scales were labeled *mistrust in military*, *physical deprivation*, *social support*, *felt overworked*, *battle experiences*, *rumination*, *chemical/biological warfare*, *food/infection/equipment*, *desert/exhaust*, and *ate local food*. The scale internal consistencies, shown at the bottom of the table, ranged from 0.71 to 0.83, indicating adequate internal consistency. The scales had moderate intercorrelations, with an absolute value mean of 0.25 and a standard deviation of 0.13. In further analysis, the first 6 scales listed above were considered war stressors and the last 4 were considered reported exposures.

Analyses of Symptom Group Differences

Table 3 shows the corrected symptom group differences with corresponding effect sizes. For continuous variables, the differences are in means; for categorical variables, the differences are in cell frequencies with odds ratios.

War Stressors. Four variables were reported at higher rates in the high-symptom group: the *mistrust in military* scale, the number of days wearing a gas mask for at least 4 hours, being wounded, and the *physical deprivation* scale. The effect sizes were small. The frequency that the groups reporting a traumatic event was different, but not less than the 0.01 significance level. The other stressors were not reported at significantly different rates.

Prophylactic Treatments. The 2 symptom groups reported receiving the botulism and anthrax vaccine injections at different rates, but not at the significance level less than 0.01. The other prophylactics were not reported at significantly different rates.

Reported Exposures. The mean reported exposures to *chemical/biological warfare*, *food/infection/equipment* and *desert/exhaust* were higher among those in the high-symptom group than in the low-symptom group. The small–medium effect size for the *chemical/biological warfare* scale was the largest of all the stressor or exposure variables. *Ate local food* was not reported at significantly different rates.

Life Events. The Fisher's protected test of the symptom groups' reported differences across the 18 life events was significant (chi-square [18,959] $= 57.62$, $P < 0.01$); the semipartial eta was 0.24, a small–medium effect size. The reported rates of change across the 18 life events over the 5 periods were also significant (chi-square [72,905] $= 108.23$, $P < 0.01$), with a medium effect size (semipartial eta $= 0.33$). The statistical significance of these tests, controlling

TABLE 1
Control Variable Descriptive Statistics

	Percent or Means					
	High Symptoms	Low Symptoms	Cell Count	Effect Size	Odds Ratio	*P*
Total sample	40%	60%	978	–	–	–
Race/ethnicity	–	–	–	.17	–	<0.01
White	34%	66%	676	–	Ref	–
Black	50%	50%	207	–	1.91	<0.01
Other	55%	45%	93	–	2.34	<0.01
Age	35.6	34.9	–	.04	–	NS
Gender	–	–	–	.04	–	NS
Male	40%	60%	894	–	Ref	–
Female	37%	63%	82	–	0.87	NS
Education ordinal scale*	3.9	4.2	–	.15	–	<0.01
Military branch	–	–	–	.08	–	NS
Army	42%	58%	689	–	Ref	–
Marines	36%	64%	136	–	0.78	NS
Air Force	34%	66%	74	–	0.71	0.19
Navy	31%	69%	54	–	0.64	0.14
Rank	–	–	–	.08	–	0.10
Enlisted	40%	60%	465	–	Ref	–
Noncommissioned officer	42%	58%	398	–	1.09	NS
Officer	28%	72%	89	–	0.60	0.04
Duty	–	–	–	.05	–	NS
Active	41%	59%	506	–	Ref	–
Reserve	36%	64%	234	–	0.84	NS
Guard	42%	58%	175	–	1.08	NS
Smoked at least 100 cigarettes	–	–	–	.12	–	<0.01
No	33%	67%	435	–	Ref	–
Yes	45%	55%	533	–	1.63	<0.01
Had 7 drinks per day for 2 weeks	–	–	–	.09	–	0.01
No	38%	62%	816	–	Ref	–
Yes	49%	51%	155	–	1.57	0.01
Used drugs more than 5 times	–	–	–	.03	–	NS
No	39%	61%	723	–	Ref	–
Yes	42%	58%	240	–	1.14	NS
Marital status at deployment	–	–	–	.12	–	0.02
Married	39%	61%	503	–	Ref	–
Single, never married	36%	64%	340	–	0.85	NS
Divorced	42%	58%	67	–	1.11	NS
Separated	59%	41%	29	–	2.18	0.04
Living with mate	62%	38%	26	–	2.47	0.03
Health at deployment ordinal scale†	1.8	1.8	–	.01	–	NS
Current PTSD symptoms ordinal scale‡	2.4	1.7	–	.32	–	<0.01

Notes: Nominal variable cell counts do not add up to 978 because of missing data (missing data cells not shown).
Effect size is multiple correlation (*R*) for continuous variables and eta for nominal variables.
Odds ratios compare the high- versus low-symptom groups in the given category compared with the referent (Ref).
* 1 = less than high school, 2 = some high school, 3 = high school diploma, 4 = some college, 5 = bachelor's degree, 6 = some graduate school, 7 = master's degree, 8 = higher-level graduate degree.
† 1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor.
‡ 1 = never or no traumatic event, 2 = rarely, 3 = sometimes, 4 = often, 5 = always.
NS, not significant; PTSD, posttraumatic stress disorder.

for potential confounders, allowed us to examine the group differences for specific life events.

Further analysis revealed that there were significant differences for both group and rate of change for 4 life events. These were: *having a serious accident/illness/medical problem*, *loved one having a serious accident/illness/medical problem, being unable to work for month or more because of illness or injury*, and *going bankrupt/having property repossessed/other serious financial problem.*

The effect sizes, semipartial etas, were greatest for group differences and rates of change differences for *being unable to work. . .* (0.17 and 0.19, respectively). The effect sizes for the other events were smaller: *having a serious accident. . .* 0.08

TABLE 2
Exposure and Stressor Items Varimax Factor Correlations

Item	Battle Experiences	Rumination	Desert/ Exhaust	Food/ Infection/ Equipment	Mistrust in Military	Chemical/ Biologic/ Warfare	Physical Deprivation	Social support	Ate Local Food	Felt Overworked
Get fired on	**.76**	.11	.01	.00	−.06	.06	.06	.00	.11	.20
Enemy weapons fire	**.71**	.12	.10	.15	−.04	.18	.02	−.03	.00	.17
Fire at enemy forces	**.66**	.09	.03	.08	−.04	.01	.10	−.08	.02	.00
Come into contact with enemy prisoners	**.59**	.01	.19	−.01	.17	.11	.14	.02	−.05	−.20
See people seriously wounded or killed	**.57**	.08	.21	.07	.14	.09	.11	.00	.03	−.15
Allied weapons fire	**.50**	.15	.12	.24	.04	.14	.07	−.08	−.04	.05
Come under a missile or artillery attack	**.45**	.10	.08	−.12	−.02	.31	.08	.05	.28	.29
Prepare for a missile or artillery attack	**.35**	.14	.16	−.06	.05	.22	.07	.09	.24	.22
Smoke from oil fires	**.30**	.06	.15	.16	.01	.27	.01	.00	−.07	.07
Worry about what might happen to you	.13	**.77**	.12	.08	.05	.07	.04	.09	.02	−.02
Unconfident of returning home safe	.17	**.71**	.06	.13	.19	.10	.09	−.04	.03	.12
Talk about getting hurt or dying	.17	**.65**	.04	.04	.05	.04	.02	.12	.04	−.05
Worry about those you love	.06	**.53**	.10	.13	.11	.02	.03	.24	−.02	.07
Worry that a relationship might break up	.05	**.45**	.03	.11	.06	−.02	.07	.01	.01	.05
Question if US involvement was right	.05	**.43**	.02	.14	.27	.08	.04	−.03	.12	.00
Feel untrained for what you encountered	.02	**.35**	.01	.05	.24	.17	.16	.05	.05	.06
Not have enough sleep	.24	**.30**	.20	.19	.23	.08	.30	−.05	.04	.14
Harsh sunlight	.06	.06	**.76**	.07	.01	.06	.07	.04	.08	.13
Very hot or cold temperatures	.07	.13	**.74**	.07	.04	.05	.09	−.01	.04	.08
Blowing sands	.17	.01	**.70**	.05	.09	.12	.06	.12	−.03	.01
Snakes, insects, or animals	.19	.06	**.55**	.30	.09	.02	.03	.03	.01	−.02
Gasoline or diesel exhaust	.16	.10	**.50**	.33	.04	.14	−.01	.02	−.02	.01
Burning trash or feces	.20	.02	**.45**	.39	.19	.10	.11	.10	−.04	−.13
Smoke from space heaters	.04	.03	**.37**	.34	.18	.14	.02	.07	.06	−.10
Contaminated or unsafe food	.11	.15	.16	**.60**	.16	.11	.21	−.03	.17	.12
Unsafe drinking water	.12	.14	.10	**.59**	.06	.09	.23	−.01	.20	.10
Communicable diseases	.09	.12	.15	**.56**	.11	.09	.13	.02	.06	.04
Faulty safety equipment	.18	.18	.12	**.50**	.18	.21	.20	−.05	.07	.06
Smoke from cigarettes	.02	.17	.28	**.46**	.08	.02	−.05	.05	.01	−.01
Microwaves	−.03	.06	.03	**.30**	.04	.11	.03	.03	.13	.10
Lack confidence in the ability of superior officers	.00	.18	.12	.09	**.67**	.07	.05	.09	.06	.07
Feel untrusting of those you served with	−.04	.20	.04	.11	**.55**	.09	.12	.06	.04	.13
Feel you (or your unit) were forgotten	.08	.19	.10	.13	**.52**	.07	.11	−.01	.16	.01
Lack adequate medical care	.09	.24	.09	.19	**.44**	.10	.32	−.01	.08	.11
Chemical warfare	.22	.08	.16	.15	.14	**.76**	.06	.01	−.01	.01
Biologic warfare	.18	.06	.13	.19	.12	**.74**	.08	−.01	.02	.01
Radiologic warfare	.17	.16	.07	.20	.08	**.54**	.09	−.12	.03	−.01
Not have enough to eat	.14	.16	.09	.20	.17	.09	**.72**	−.05	.04	.05
Not have enough to drink	.24	.13	.06	.21	.17	.12	**.72**	−.06	.05	.06
Have a hard time keeping clean	.29	.20	.27	.22	.22	.00	**.43**	.00	−.03	.02
Receive mail from friends/family	−.01	.04	.06	.03	.05	−.04	−.02	**.72**	.05	.01
Write or send mail to friends/family	−.02	.10	.03	.04	−.01	−.07	−.01	**.72**	.03	−.01
Call friends/family	−.10	.10	.04	.08	.01	.04	−.04	**.48**	.16	−.04
Eat local food not supplied by military	.00	.07	.06	.20	.11	−.02	−.02	.11	**.67**	−.04
Drink local water not supplied by military	.09	.04	−.02	.19	.11	.02	.09	−.02	**.61**	.06
Work harder than others	.12	.13	.08	.26	.31	.02	.10	−.01	.05	**.56**
Given more difficult duties than others	.16	.19	.08	.25	.36	.02	.11	.00	−.01	**.54**
Scale internal consistency	*.83*	*.80*	*.81*	*.77*	*.74*	*.81*	*.77*	*.71*	*.71*	*.81*

Note: Bold loadings signify items added together for scale.
Scale internal consistencies are Cronbach's alpha.

TABLE 3
Adjusted Symptom Group Mean and Percent Differences for Self-Reported Exposures and Stressors

	No.	Means or Percent "Yes" High Symptoms	Low Symptoms	Effect Size	Odds Ratio	*P*
	War Stressors					
Mistrust in Military*	910	2.90	2.50	.14	—	<0.01
Days gas mask worn for at least 4 hours	892	12.96	8.05	.12	—	<0.01
Wounded	964	17%	10%	.10	1.84	<0.01
Physical deprivation*	965	2.83	2.54	.09	—	<0.01
Experienced a traumatic event	956	57%	62%	.07	0.77	0.03†
Social support*	955	3.96	4.12	.06	—	0.06
Felt overworked*	960	2.88	2.68	.06	—	0.08
Days gas mask worn for any time	894	27.90	24.09	.05	—	0.12
Battle experiences*	900	3.14	3.02	.05	—	0.15
Rumination*	938	3.04	2.93	.04	—	0.17
	Prophylactic Treatments					
Botulism vaccine (injection)	322	77%	66%	.13	1.78	0.02†
Meningococcus vaccine	261	78%	70%	.10	1.57	0.10
Anthrax vaccine (injection)	621	88%	81%	.08	1.72	0.03†
Days taking any PB pills	770	12.04	9.27	.06	—	0.07
Days taking >3 PB pills	768	3.28	1.97	.06	—	0.08
Plague vaccine	415	84%	80%	.06	1.31	NS
Typhoid vaccine (injection)	656	95%	93%	.05	1.43	NS
Ciprofloxacin (antianthrax pill)	426	69%	66%	.03	1.14	NS
Immune globulin (IG gamma globulin)	677	95%	94%	.03	1.21	NS
Total known prophylactics (not PB)	900	3.69	3.57	.03	—	NS
Malaria pills	679	65%	65%	.01	1.00	NS
	Reported Exposures					
Chemical/biologic warfare*	856	3.35	2.60	.24	—	<0.01
Food/infection/equipment*	894	3.30	2.87	.16	—	<0.01
Desert/exhaust*	919	5.52	5.20	.12	—	<0.01
Ate local food*	961	2.43	2.26	.06	—	0.06

Notes: Race, age, gender, education, military branch, military rank, military duty, marital status at deployment, health at deployment, alcohol use, smoking, drug use, and PTSD symptoms are partialed out.

Effect size is semipartial multiple correlation (*R*) for continuous variables, and semipartial eta for nominal variables. Odds ratios compare the high- versus low-symptom groups in the given category.

* 7-point scale: 1 = not at all or never, 4 = moderately or sometimes, 7 = extremely or always.

† $P \leq 0.05$, but greater than the planned comparison probability of <0.01.

PB, pyridostigmine bromide; NS, not significant; PTSD, posttraumatic stress disorder.

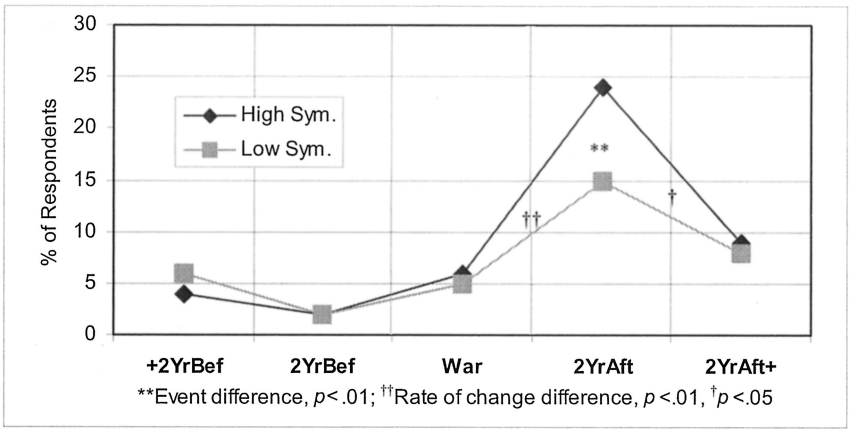

Fig. 1. Percent of respondents endorsing having a serious accident/illness/medical problem.

and 0.11; *loved one having a serious accident*. . . 0.11 and 0.13; *going bankrupt*. . . 0.11 and 0.14.

Data for the 4 life events are shown in Figures 1 through 4. They form a general pattern in which there was: 1) no or a slight difference between the symptom groups before and during the war, 2) the high-symptom group reporting the event at a relatively higher rate in the 2 years after the war, and then 3) this rate declining during the last period to a rate similar to the low-symptom group's. An exception to this is that for *loved one having a serious accident*,. . . there were also differences between the groups before the war, although not during the war (see Fig. 2).

The 2 symptom groups did not significantly differ for the other life events. These included: *marriage, divorce/separation or breakup of a*

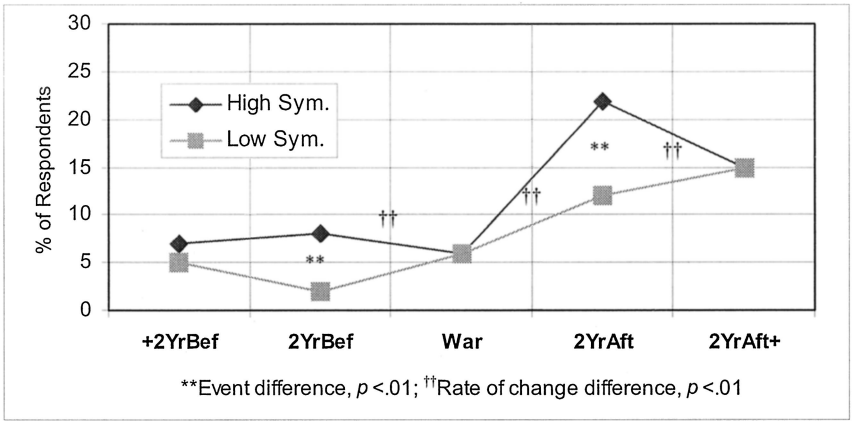

Fig. 2. Percent of respondents endorsing a loved one as having a serious accident/illness/medical problem.

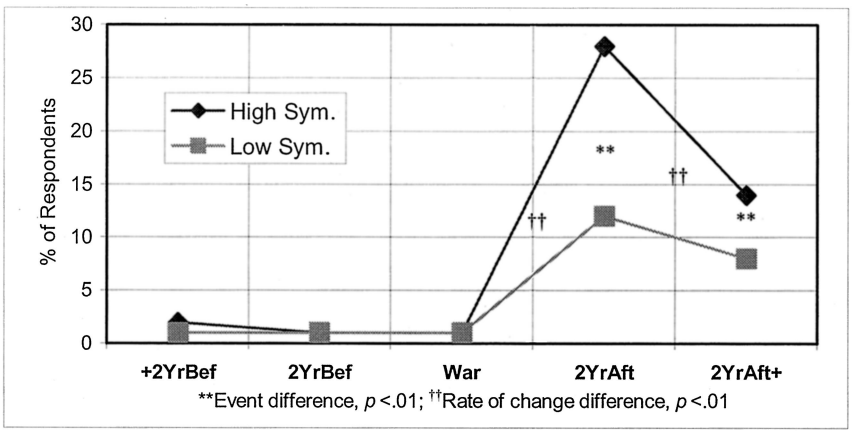

Fig. 3. Percent of respondents endorsing being unable to work a month or more because of illness or injury.

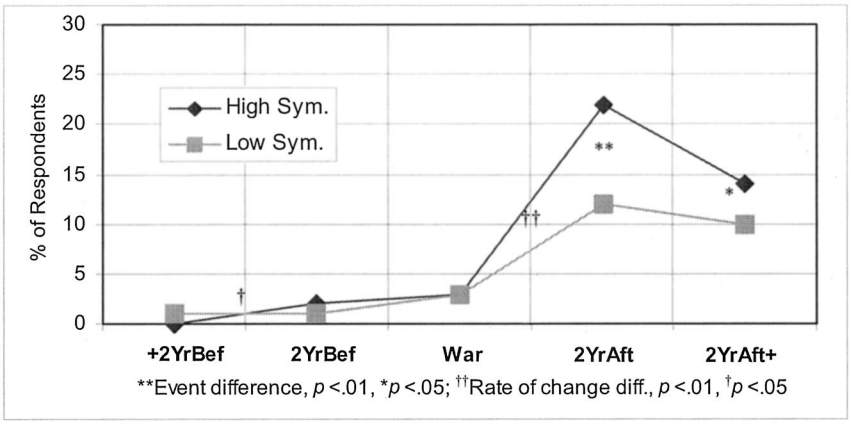

Fig. 4. Percent of respondents endorsing going bankrupt/having property repossessed/other serious financial problem.

long-term relationship, job change, promotion, demotion, death of a loved one, birth of a child, property loss from robbery or fire or natural disaster, physical/sexual assault, loved one experiencing physical/sexual assault, starting or graduating from school, quitting school, buying/selling a house, and *involved in a lawsuit.*

Discussion

The 2 groups of veterans differed in important ways concerning reported exposures, life events, and war-related stressors. Most prominent were greater perceived exposures to chemical/biologic warfare and increased levels of occupational disability after the war reported by those in the high-symptom group.

Possible exposures to chemical/biologic weapons has been an important concern of veterans, government, and media since returning soldiers first began reporting medically unexplained symptoms in 1991. Our findings suggest that such reported exposures are an important element of the medically unexplained symptoms, which have persisted after the Gulf War. These findings are in agreement with previous studies.[7,11,14,30]

We may never conclusively know if allied troops were significantly exposed to chemical/biologic weapons during the Gulf War. However, substantial evidence supporting a medically significant exposure is presently limited, as is the likelihood of an exposure leading to the current clinical presentation.[1]

In light of this, we hypothesize that, if there was not a significant exposure, the belief of being exposed would be the important element behind this relatively powerful predictor of unexplained symptoms. The way this belief might cause or magnify symptoms is not well understood, but likely works through several pathways.[31] Vyner[32] points out that the uncertainty of possibly being exposed to toxic elements that are environmentally or medically invisible can lead to enduring cognitive, emotional, and behavioral problems. One possibility is that the belief of having been exposed led to increased symptoms. Another is that some veterans who began experiencing unexplained symptoms as a result of war stress and trauma made post-hoc attributions that they must have been exposed. The connection between the belief in exposure to chemical/biologic warfare and unexplained symptoms is a critical area for further investigation, both for Gulf War

and other unexplained symptom outbreaks in general.

Whatever the cause of the symptoms in some Gulf War veterans, being ill is associated with a negative impact on both their and their families' lives. Approximately one fourth of the high-symptom group reported inability to work because of disability at times in the 2 years after the war. Another one fourth reported a serious accident, illness, or medical procedure. Given this, it is not surprising that over 20% of the high-symptom group reported financial difficulty during the same period.

That a loved one, presumably a family member, of over 20% of the high-symptom group also became ill or was an accident victim in the 2 years after the war underscores the importance of better understanding the trauma of war. It has been pointed out that illness in 1 family member usually affects the lives of the others.[33] Although our data suggest that these family members were also more ill before war, it is notable that there were no differences in reported family illness during the war, and that the group discrepancy was substantially greater after the war.

Although there were more negative life events reported in the 2 years after the war for veterans in the high-symptom group, it is important to note that reports of these significantly decreased in the years subsequent to 2 years after the war. These data were collected in 1995; further study extending this trend would shed light on whether the negative events occurred at different rates over a longer timeframe after the war.

The reported attitude of mistrust toward the military might function as both a proxy for having a worse experience while in the Persian Gulf and as a cause of symptoms. It is well established that pessimism predicts illness.[34] The *mistrust in military* scale had a moderately high correlation with the *physical deprivation* scale, which was also elevated for high-symptom veterans. This suggests that these veterans could well have had more difficult day-to-day experiences while in the Persian Gulf. However, it is also possible that respondents were biased in their recall of events. It is ultimately impossible to distinguish between the respondents' actual experiences and their memory of the events.

The high-symptom group veterans were reported greater exposure to possible infection and unsafe equipment. Fiedler et al.[14] found that veterans who had experienced equipment failure that jeopardized safety had increased symptoms. The infection aspect of the scale was composed of items dealing with unsafe food and water, and communicable disease. Although judgments regarding the safety of food and water are likely more subjective than some others, some upper respiratory and gastrointestinal infections were known to occur among deployed troops at increased rates.[12]

We found that exposure to desert conditions was associated with being in the high-symptom group. This suggests that nonpsychosocial stress could play an important role in Gulf War symptoms. An additional component of this scale was smoke from engines or other sources in the field, which other studies[7,11,30] found to be associated with increased symptoms.

Gulf War veterans often describe wearing a gas mask during particularly stressful and fear-inducing conditions. Thus, the association of number of days wearing a gas mask with higher symptom levels is consistent with these veterans also having the most stressful experiences during the war. Furthermore, we assume the finding that there were more high-symptom group veterans who reported being wounded also reflects their being in the most stressful war situations, although the nature of these wounds is unclear.

We did not find significant associations with either variable measuring reported number of days taking PB pills and symptom group membership. This is consistent with Proctor et al.[7] who also controlled for, among other things, PTSD and education. Cherry et al.[4] did find an association between reports of taking PB pills and subsequent symptoms, but this finding was corrected only for military branch.

As a result of the exploratory nature of our study, we did not find associations of reported botulism or anthrax vaccines with group membership at significance levels exceeding that set before analyses. However, these associations would have been significant if they had been hypothesized beforehand, and more study of the association of these vaccines with symptoms is needed. Unlike Unwin et al.,[11] the plague vaccine was not associated with group membership. The total number of vaccinations was not significantly related to symptom group membership; however, we were not able to make the distinction of before deployment versus during deployment that Hotopf et al.[10] did when finding their association.

Although the differences between the symptom groups cannot be attributed to the demographic and other variables controlled for, it is important to note again that differences could be the result of veterans who had higher symptoms being biased in their recall of exposures, stressors, and life events. Veterans who report more symptoms and perceive themselves to be ill could consequently recall more exposures and stressors.

Another caveat is that although we did not assess or control for existing medical conditions, which could contribute to veterans' symptoms, all veterans had been examined as part of the Registry process. These diagnoses largely did not explain the reported symptoms[1]; Fukuda et al.[5] found a similar result for a smaller group studied with concurrent physical examinations. Hallman et al.[16] found that self-reported medical and psychiatric diagnoses are relatively poor predictors of being in the high-symptom group. Explanations for

these symptoms clearly go beyond standard medical and psychiatric diagnoses.

In conclusion, there are important differences between the high- and low-symptom groups that suggest that the belief of being exposed to chemical/biologic weapons is an important concomitant of, and perhaps contributor, to the symptoms known as Gulf War illness. More essential is that, regardless of the cause of their symptoms, ill veterans reported experiencing from more negative life events in the years immediately after the war.

To understand how soldiers' health and perceptions of health become compromised, we need to have a better understanding of the types of exposures soldiers experience during deployment and their perceptions of those exposures. Adding psychosocial variables to biologic models is increasingly warranted as we investigate largely symptom-based illness after war.

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