

The epidemiology of illness in PGWV is not the focus of this report and indeed is the subject of a separate RAND effort. This chapter provides a summary of some factors related to epidemiology, but it is in no way intended to be a complete review of the epidemiological data.

PGWV REPORT HEALTH PROBLEMS

Many PGWV (approximately 100,000) have participated in health registries through the Veterans Administration (VA) or DoD, and most of them report having health problems. A variety of studies have characterized their symptoms and diagnoses. Table 3.1 shows, as an example, the most frequent principal diagnoses in PGW registry personnel as of February 1997 (N = 74,653). The findings, while generally consistent, vary somewhat with the wording and category boundaries employed to define the symptoms and diagnoses.

SYMPTOMS IN PGWV

Findings reported here are taken from a single study of symptoms in PGWV (Roy et al., 1998); findings from other studies evaluating symptoms are qualitatively similar. "Signs, symptoms, and ill-defined conditions" (SSID) constituted the primary diagnosis for 17.2 percent of the veterans and the primary or secondary diagnosis for 41.8 percent.

Although the authors state that "more definitive, often psychological, diagnoses can be made by increasing the intensity of the evaluation and by multidisciplinary input," no evidence was provided that psychological diagnoses would be made on intensive scrutiny at a higher rate in PGWV than in non-PGW personnel, or in personnel without symptoms (or perhaps those for whom symptoms were falsely assigned to deal with the possibility that diagnoses may be made precisely because of illness reporting).

Table 3.1
Most Frequent Principal Diagnoses in PGW Registry Personnel,
February 1997
(N = 74,653)

Symptom	Frequency (%)
No diagnosis	22.8
Missing diagnosis	5.1
Pain in joints	4.0
Complaint for which no diagnosis was made	2.7
Psychalgia	2.0
Other specified adjustment reaction	1.9
Depressive disorder, not elsewhere classified	1.8
Contact dermatitis and other eczema, unspecified cause	1.6
Asthma, unspecified	1.6
Lumbago	1.6
Essential hypertension	1.5
Migraine	1.5
Malaise and fatigue	1.4
Allergic rhinitis, cause unspecified	1.3
Unspecified sinusitis (chronic)	1.3
Other and unspecified non-infectious gastroenteritis and colitis	1.3
Osteoarthritis, unspecified	1.1
Sleep disturbance	1.0
Irritable colon	0.9
Alopecia	0.9
Anxiety states	0.8
Headache	0.7

Source: Roy et al. (1998).

COMMENT ON HEADACHE

Of the subjects who had a primary diagnosis of headache, 35 percent were categorized as migraine (classified as neurological), 38 percent as tension (classified as psychological), and 27 percent as ill-defined SSID (Roy et al., 1998). There was also wide variation in diagnosis by region, with migraine diagnosed in 23 percent to 50 percent of all veterans, tension in 19 percent to 48 percent, and SSID in 4 percent to 41 percent (Roy et al., 1998). Table 3.2 lists the symptoms in order of prevalence.

In those with a primary diagnosis of good health, prevalences were as shown in Table 3.3.

Symptom prevalence for those given a diagnosis other than SSID (Table 3.4) and those diagnosed with SSID (Table 3.5) is qualitatively similar, and roughly

Table 3.2
Symptom Prevalence as Primary and Any Diagnosis

Symptom	Primary Diagnosis (%)	Any Diagnosis (%)
Fatigue	26.8	30.3
Headache	14.5	21.3
Sleep disorders	11.7	19.0
Memory loss	9.9	16.9
Sleep apnea	7.4	5.5
Rash	3.8	5.7
Dyspnea	4.7	8.0
Chest pain	2.4	3.9
Digestive	1.8	2.6

Source: Roy et al. (1998).

Table 3.3
**Symptom Prevalence in Subjects with a Primary
 Diagnosis of Good Health**

Symptom	Percentage
Fatigue	20.7
Joint pain	20.1
Headache	12.5
Sleep disturbance	11.2
Memory loss	14.7
Problems concentrating	9.2
Rash	10.9
Depressed mood	7.1
Muscle pain	6.7
Diarrhea	6.7
Hair loss	5.9
Dyspnea	4.9
Abdominal pain	5.3
Bleeding gums	3.6

Source: Roy et al. (1998).

similar in ordering, to that of other reports on symptoms in ill PGWV. Results from other studies are not reviewed here.

INCREASED SYMPTOM REPORTING IN PGWV

Many of the problems reported by ill PGWV also occur in the general population. It is desirable to know whether and to what degree PGWV experience higher rates of illness than others. Several studies have shown that those deployed to the Gulf have higher rates of self-reported physical symptoms

Table 3.4
Symptom Prevalence in Subjects Given a
Diagnosis Other Than SSID

Symptom	Percentage
Fatigue	47.1
Joint pain	55.7
Headache	41.7
Sleep disturbance	34.6
Memory loss	35.6
Problems concentrating	27.9
Rash	32.2
Depressed mood	24.0
Muscle pain	23.7
Dyspnea	20.7
Diarrhea	19.2
Abdominal pain	17.9
Hair loss	13.2
Bleeding gums	9.1
Weight loss	7.2

Source: Roy et al. (1998).

Table 3.5
Symptom Prevalence in Subjects Diagnosed
with SSID

Symptom	Percentage
Fatigue	59.5
Joint pain	47.4
Headache	44.3
Sleep disturbance	41.0
Memory loss	40.6
Problems concentrating	31.1
Rash	29.8
Depressed mood	21.5
Muscle pain	21.5
Dyspnea	20.2
Diarrhea	18.0
Abdominal pain	15.6
Hair loss	13.0
Bleeding gums	8.5

Source: Roy et al. (1998).

than those who were not deployed (Centers for Disease Control and Prevention, 1995; Stretch, 1995; Iowa Persian Gulf Study Group, 1997; Canadian Department of National Defence, 1998; Fukuda et al., 1998; Wolfe et al., 1998). Symptoms commonly reported by deployed veterans are those that might be expected from the diagnoses: fatigue, joint pain and stiffness, diarrhea, un-

refreshing sleep or sleep difficulties, diarrhea and abdominal discomfort, weakness, cognitive symptoms (e.g., difficulty remembering, problems with word finding, or impaired concentration), headaches, and weakness. Some recent efforts have been made to devise case definitions. One researcher has articulated case definitions for each of three syndromes identified by factor analysis (Haley, 1997). Another working definition requires symptoms in two of three major categories of fatigue, musculoskeletal symptoms, and mood-cognition (Fukuda et al., 1998).

The CDC conducted a study that evaluated symptoms in an Air National Guard unit from Pennsylvania (Unit A) and three comparison units from Pennsylvania and Florida chosen for similarity in mission responsibility (Centers for Disease Control and Prevention, 1995). A total of 3,927 personnel from four units participated in a survey, with response rates from 36 percent to 78 percent. In all units, the prevalence of each of 13 chronic symptoms (lasting six months or more) was significantly greater among subjects deployed to the Gulf than among those not deployed. The symptoms most frequently reported and considered “moderate” or “severe” included fatigue (61 percent), joint pain (51 percent), nasal or sinus congestion (51 percent), diarrhea (44 percent), joint stiffness (44 percent), unrefreshing sleep (42 percent), excessive gas (41 percent), difficulty remembering (41 percent), muscle pain (41 percent), headaches (39 percent), abdominal pain (36 percent), general weakness (34 percent), and impaired concentration (34 percent). The prevalence of five symptom categories—diarrhea, other gastrointestinal (GI) complaints, difficulty remembering or concentrating, “trouble finding words,” and fatigue—was significantly greater among those deployed from Unit A than among those from the other units. Both self-report and selective participation could have biased these results, however.

A second, more complete evaluation of the cohorts examined by the CDC entailed a cross-sectional survey of 3,273 currently active volunteers from four Air Force units (including 1,155 PGWV and 2,520 non-deployed personnel), together with a cross-sectional clinical evaluation of 158 PGWV from one unit, irrespective of health status (Fukuda et al., 1998). A working case definition was determined in which criteria were satisfied for a case if one or more chronic symptoms were present from at least two of three categories: fatigue, mood-cognition, and musculoskeletal symptoms. Severe cases were those in which there were “severe” symptoms from each category. A factor-derived case was defined as one in which the combined factor score was in the top 25 percent of questionnaire responses, including those of non-PGWV. Forty-five percent of PGWV and 15 percent of non-deployed personnel were symptom-category cases. Forty-seven percent of PGWV and 15 percent of non-deployed personnel were factor-score cases. This suggests that the authors selected the 25 percent

cutoff to match the symptom-derived cases. The authors stated that the syndrome should be such that it embraces at least 25 percent of PGWV, but this is at once arbitrary and inappropriate: 25 percent of legionnaires or Four Corners residents would obviously not need to be ill for *Legionella pneumonia* or hantavirus to have produced an illness syndrome in those groups. For symptom-derived cases, 39 percent of PGWV and 14 percent of non-deployed personnel met criteria for mild to moderate illness; 6 percent vs. 0.7 percent met criteria for severe illness. Illness was reportedly not associated with time or place of deployment or with duties during ODS/DS. There were no differences in lifetime reports of 35 medical and psychiatric conditions, including heart disease, hypertension, diabetes, alcohol and substance abuse, anorexia/bulimia, migraine or severe headache, anxiety, diarrhea, irritable bowel syndrome, or impotence. History of prior depression was significantly more common in severe cases (15 percent) than in non-severe cases (0 percent, $p < 0.05$). Severe illness was associated with Gulf War service, female sex, enlisted rank, and smoking, on multivariate analysis. There was no association between illness and number of deployments, month/season of deployment, duration of deployment, military occupational specialty, direct participation in combat, or self-reported locality in the Gulf region (most of the respondents had been in Riyadh).

The Iowa Persian Gulf Study Group (1997) assessed the prevalence of self-reported symptoms in Iowa PGWV and non-deployed personnel. Of 238,968 persons, 4,886 were randomly selected from one of four groups: Gulf-deployed active-duty military, Gulf-deployed National Guard/Reserve, non-Gulf-deployed active-duty military, and non-Gulf-deployed National Guard/Reserve. A total of 3,695 subjects completed a telephone interview. Symptom reporting was higher for Gulf-deployed veterans for fibromyalgia (19.2 percent vs. 9.6 percent), cognitive dysfunction (18.7 percent vs. 7.6 percent), alcohol abuse (17.4 percent vs. 12.6 percent), depression (17 percent vs. 10.9 percent), asthma (7.2 percent vs. 4.1 percent), anxiety (4.0 percent vs. 1.8 percent), bronchitis (3.7 percent vs. 0.8 percent), post-traumatic stress disorder (PTSD) (1.9 percent vs. 0.8 percent), sexual discomfort (1.5 percent vs. 1.1 percent), and chronic fatigue (1.3 percent vs. 0.3 percent).

Another group distributed 16,167 survey questionnaires, of which 31 percent were returned; PGWV reported significantly more of each of 23 physical health symptoms than non-deployed veterans, an effect not significantly altered by controlling for smoking and drinking, age, rank, education, marital status, and branch of military service (Stretch et al., 1995, 1996a,b).

A study of exposures and symptoms in PGWV from a Fort Devens ODS Reunion Survey did not include a non-deployed control group but found that the five

most commonly reported symptoms among the 2,119 subjects who returned the survey (of 2,313 surveyed) were aches/pains, lack of energy, headaches, insomnia, and feeling nervous/tense (Wolfe et al., 1998). PTSD was associated with health symptoms, but subjects with combat exposure were not more likely to report increased health symptoms.

A survey was sent to all Canadian PGWV and a sample of those serving elsewhere during the Gulf War, a total of 9,947 personnel. The survey, returned by 3,113 PGW-deployed (73 percent of those solicited) and 3,439 non-deployed (60.3 percent), found that PGWV reported higher prevalences of symptoms of chronic fatigue, cognitive dysfunction, multiple chemical sensitivity, major depression, PTSD, anxiety, fibromyalgia, and respiratory diseases (bronchitis and asthma together) (Canadian Department of National Defence, 1998). It also found higher numbers of children with birth defects (before, during, and after the PGW).

Because these studies are based on self-reported illness, it is possible that reporting bias and self-selection could have influenced results. Although the degree to which these factors may influence self-reported symptomatology is unknown, it can by no means be assumed that bias serves as the sole explanation for the higher rates of symptom reporting by personnel deployed to the Persian Gulf.

FACTORS ASSOCIATED WITH REGISTRY PARTICIPATION

Determination of what constitutes the cause or causes of illness may be helped by analysis of factors associated with illness development. Registry participation is not equivalent to illness, since many PGWV who have not participated in registries report health problems, and some who have participated in registries report no health problems. However, a rough relationship between illness and registry participation is present. Table 3.6 shows predictors of registry participation and their associated odds ratios (Gray, 1996).

The degree to which predictors of registry participation predict illness as opposed to inclination to participate can be determined only by evaluating these predictors against more definitive criteria for illness. Indeed, some studies cite increased participation of reservists, who in one account represented nearly half of those reporting health problems, while making up only 17 percent of the troops serving in the PGW (Thompson, 1996). However, "the Pentagon attributes this discrepancy to the reluctance of active-duty soldiers to complain for fear of losing their jobs in a shrinking military, on the reservists' greater age and on the fact that the war disrupted their lives more severely than those of active-duty troops" (Thompson, 1996).

Table 3.6
Registry Participation Predictors

Factor	Odds Ratio
Stationed in PGW theater	2.2
Age: younger than 31/older than 22	2.1
Enlisted	2.0
Construction worker	1.3
Female	1.3
Hospitalized during 12 months prior to PGW	1.2
Army	4.7 (4.6–4.9)
National Guard	2.6 (2.5–2.6)

Source: Gray (1996).

INFORMATION FROM EPIDEMIOLOGICAL INVESTIGATIONS OF SELF-REPORTED PESTICIDE EXPOSURE AND ILLNESS

No definitive link has been found between self-reported pesticide exposure and illness in PGWV. Two factors have complicated determination of such a link: Both outcome data and information on exposures have been poor. Some information from epidemiological studies is available, and this information is consistent with the possibility of a link between self-reported pesticide exposure and illness, although it does not prove a causal connection.

Epidemiological studies performed on members of a Naval Reserve construction battalion (CB24) reported to have a high rate of PGW-attributed symptoms were surveyed for symptoms and for exposures. Three primary syndromes were identified, which were termed Syndrome 1 (impaired cognition), Syndrome 2 (confusion ataxia), and Syndrome 3 (arthro-myo-neuropathy). Syndrome 1 was correlated with the use of pesticide-containing flea and tick collars and pesticide applications in encampments ($p < 0.001$), and Syndrome 3 was related to heavy use of military-supplied insect repellent (DEET, 75 percent in ethanol) ($p < 0.001$) (Haley and Kurt, 1997a,b; Kurt, 1998). In addition, Syndrome 2 was correlated with chemical alarms ($p < 0.001$) and being in a sector later suspected to have potential nerve-agent exposure ($p < 0.04$). The provisos associated with self-report suggest that there may be increased recall of an exposure by those who are ill; however, there is no cogent rationale for presuming that these different syndromes would be systematically and differentially linked to these exposures (with one syndrome leading to amplified recall of one exposure, and another to amplified recall of a different exposure). If these relationships are preserved in a replication sample, this would provide credence to a possible link between pesticides (potentially including OPs) and Syndrome 1.

Another report found that among British servicemen (findings for men only were reported), service in the PGW was associated with increased incidence of

illness (using a description of an “empiric multisystem syndrome” for Gulf War illnesses [Fukuda et al., 1998]) based on comparisons with Bosnia and non-deployed PGW-era cohorts: an odds ratio of 2.5 (2.2 to 2.8) (Unwin et al., 1999). Among PGW, Bosnia, and PGW-era cohorts, 61.9 percent, 36.8 percent, and 36.4 percent met the working PGW illness criteria, respectively, with 25.3 percent, 11.8 percent, and 12.2 percent meeting criteria for severe symptoms. As shown in Table 3.7, various self-reported exposures were associated with illness in PGWV. In particular, self-reported exposures to pyridostigmine bromide (PB) and pesticides by British veterans were associated with increased odds ratios for the empiric multisystem syndrome of chronic, multisymptom, ill-defined illness. While the odds ratios for personal pesticide use and pesticides on clothes/bedding were high among the factors examined, it is interesting that these odds ratios are comparable for the three study groups for these and all other exposures examined. Recall and reporting bias remain possibilities, and many other exposures were also apparently associated with likelihood of illness.

In summary, many PGWV report health problems, and there is some consistency in the health problems reported among PGWV cohorts. Further, reporting of health problems occurs at a higher rate among PGWV than among other veterans. Self-reported exposures, including those to pesticides, in the PGW are associated with increased likelihood of illness. The likelihood that this is the result of recall bias in ill veterans is reduced by information showing that comparable odds ratios are seen for risk factors for which records are available for

Table 3.7
Odds Ratios for CDC-Defined PGW Illnesses in PGWV and Bosnia and
Non-Deployed Gulf-Era Veterans
(95 percent confidence interval)

Factor	PGW Veterans	Bosnia Veterans	PGW-Era, Non-deployed
PB	2.6 (2.2–3.1)	3.4 (1.7–6.8)	1.9 (1.4–2.8)
Pesticides on clothes or bedding	1.9 (1.6–2.2)	1.7 (1.4–2.2)	1.9 (1.5–2.3)
Personal pesticides	2.2 (1.9–2.6)	1.8 (1.5–2.2)	1.8 (1.5–2.2)
Exhaust from heaters or generators	1.9 (1.6–2.2)	2.8 (2.1–3.7)	2.4 (1.9–2.8)
NBC suits	2.7 (2.3–3.3)	2.7 (1.6–4.8)	2.3 (1.5–3.7)
Anthrax vax	1.5 (1.3–1.7)	1.5 (0.7–2.9)	NA
With records	1.4 (1.0–1.8)	2.6 (0.9–7.4)	NA
Any biological	1.5 (1.3–1.7)	1.5 (0.8–2.8)	NA
With records	1.4 (1.1–1.9)	2.5 (0.9–6.6)	NA
Yellow fever	1.3 (1.1–1.7)	1.0 (0.7–1.4)	NA
With records	1.4 (0.9–2.0)	0.8 (0.5–1.2)	NA
Tetanus	1.3 (1.1–1.5)	1.0 (0.8–1.3)	NA
With records	1.1 (0.8–1.4)	1.0 (0.7–1.3)	NA
Any routine	1.2 (1.1–1.4)	1.1 (0.9–1.3)	NA
With records	1.0 (0.7–1.3)	1.0 (0.7–1.3)	NA

NA = not available.

some (British) veterans. However, there is insufficient evidence to clearly define a causal link between self-reported pesticide exposure and increased likelihood of illness. If the existence of such a link is to be adequately examined, it will be necessary to conduct studies with replication samples of those reviewed above. There is also a need for more detail regarding health effects experienced by PGWV. The broad categories of effects in many current surveys often do not permit a determination of whether the symptoms can be logically associated with particular agents, such as pesticides, with or without more complete exposure data. Until more information is available on the symptoms and their context, the value of the surveys in terms of identifying a causal agent (or agents) will always be limited.