THE EFFECTS OF MUSTARD GAS, IONIZING RADIATION, HERBICIDES, TRAUMA, AND OIL SMOKE ON US MILITARY PERSONNEL: The Results of Veteran Studies

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INTRODUCTION

As an occupational group the men and women in the United States military perform a wide range of tasks in a wide variety of settings. One aspect of their duties that distinguishes them from most other occupational groups is the degree of risk to which they are exposed in time of war. Their service to their country is recognized not only by monetary rewards, but also by a commitment to their health and well-being. This commitment to the health of the military is related to both maintaining an efficient and ready force and to identifying health hazards they may encounter in the line of duty. The latter aspect of health surveillance is especially pertinent when discussing veterans or those who are no longer on active duty. The Department of Veterans Affairs (VA) was created in recognition of the national service performed by veterans.

Among the charges of VA are defining the veteran population and providing health care and other benefits, some of which may be compensation for health problems that are the direct result of their military service.

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Data and findings derived from surveys and epidemiological studies of veterans enable VA to better allocate resources and compensate for service connected health problems.

Veteran research is of value to both veterans and nonveterans. Findings from research on veteran groups may be generalizable to certain groups of the general population with similar exposures or experiences. For example, studies of veterans exposed to vaccines (yellow fever), environmental hazards (malaria), or occupational hazards (herbicides, ionizing radiation), or trauma may have implications for civilians likewise exposed.

Their unique characteristics make veterans a good target population for health research. Among those characteristics that both facilitate health surveillance and enhance their desirability as a study group is that they are a readily defined cohort. Cohort studies are one of the most valuable tools in testing hypotheses regarding causation of diseases. A cohort is defined by some shared characteristic(s) present prior to the disease under investigation. The cohort is observed over a period of time to determine, among other things, the frequency of disease. Thus, a veteran cohort, based on date of entering active duty, constitutes a readily defined group in terms of sex, race, age, and exposure, all important factors in any health study.

Veterans research is further enhanced by the availability of their active duty records and veterans records maintained by the Department of Defense (DOD) and VA. The ready availability of records not only facilitates development of a study cohort but also facilitates a high degree of follow-up without great expense.

An important characteristic unique to veterans is the “healthy veteran effect”. The mortality of veterans after separation from service has been documented as lower than that of a similar age group of nonveterans (61, 63). The “healthy veteran effect” is related to the physical examination required at induction into military service, which screens those with health problems from entering the service. The military also provides physical health programs to increase both retention and readiness of its forces. Therefore, a comparison of a veteran cohort to general population may lead to a bias and should be viewed with caution.

This article aims to provide a current review of efforts both to define the veteran population and to identify specific health problems of selected veteran populations.

PROFILE OF US VETERANS

1987 Veteran Survey
The most recent and comprehensive accounting and analysis of the veteran population in the United States is based on the 1987 Survey of Veterans
Table 1  Selected military service characteristics by period of service among veteran population

<table>
<thead>
<tr>
<th>Military Service</th>
<th>WWII %</th>
<th>Korea %</th>
<th>Vietnam %</th>
<th>Post Vietnam %</th>
<th>Peace Time %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Entry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drafted</td>
<td>52</td>
<td>32</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enlisted</td>
<td>47</td>
<td>67</td>
<td>76</td>
<td>98</td>
<td>72</td>
</tr>
<tr>
<td>Rank</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commissioned officer</td>
<td>12</td>
<td>11</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warrant officer</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>.5</td>
</tr>
<tr>
<td>Enlisted</td>
<td>86</td>
<td>87</td>
<td>89</td>
<td>95</td>
<td>92</td>
</tr>
<tr>
<td>Length of Service</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 Yr.</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>1–2 Yrs.</td>
<td>37</td>
<td>34</td>
<td>31</td>
<td>22</td>
<td>46</td>
</tr>
<tr>
<td>3–5 Yrs.</td>
<td>46</td>
<td>37</td>
<td>41</td>
<td>65</td>
<td>40</td>
</tr>
<tr>
<td>6–10 Yrs.</td>
<td>4</td>
<td>7</td>
<td>10</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>11–+ Yrs.</td>
<td>7</td>
<td>19</td>
<td>15</td>
<td>.3</td>
<td>.5</td>
</tr>
<tr>
<td>Combat Exposure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposed to combat</td>
<td>52</td>
<td>35</td>
<td>38</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Served in combat zone</td>
<td>18</td>
<td>13</td>
<td>10</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Not in combat or war zone</td>
<td>29</td>
<td>50</td>
<td>50</td>
<td>92</td>
<td>84</td>
</tr>
</tbody>
</table>

*Based on a sample of 26,143,000 veterans in 1987 survey (73)

Note: percentages may not add up to 100 as veterans may have served in more than one conflict and percentage of missing values not included in table.

conducted by the Census Bureau for VA (73). The survey was conducted between July and September, 1987, and provided information to evaluate current veteran programs and plan for the future.

Based on the US Bureau of Census counts taken between April 1986 and January 1987 there were 26,143,000 veterans residing in the United States, or approximately 15% of the total US population age 20 or older. Veterans in the survey were a weighted sample of that 1987 veteran population. Selected military service characteristics of the veterans surveyed in 1987 are presented in Table 1.

Additional data captured by the 1987 survey included health problems experienced by veterans. Due to the disparities in age composition of the different groups of veterans, WWII veterans had the highest percentage reporting health problems and disability (43%), followed by Korean veterans (30%), other peace time veterans (22%), Vietnam veterans (20%), and finally post-Vietnam veterans (11%).
Of the various veteran groups today, women veterans have been receiving increased attention by the media, health researchers, and Congress. During WWII 3% of all veterans were women compared to 7% of all post-Vietnam veterans. In 1972, the last year of the draft, approximately 45,000 women were on active duty, increasing to 120,000 in 1976, and to 200,000 in 1985, when women comprised 10% of the active forces. Commensurate with the increased number of women in the military has been change in their duties. Three out of four of the 12,600 women officers in the military in 1972 were nurses. By 1985, the largest segment of the female officer population held positions other than nursing. Finally, the recent decision by the Department of Defense to allow for women combat pilots is a further indication of the changing role of women in the military.

1984 Women Veterans Survey

The Veterans Administration sponsored a survey of women veterans in 1984 to aid in evaluating current programs and to plan for the increasing number of women veterans (72). Thirty-six percent of the 3000 women veterans surveyed were under 35, which is comparable to the 31% of all veterans and 36% of the total population under 35 in the 1987 survey. The racial composition of the women veterans, of which 87% were white, was similar to that reported for all veterans and the total US population in 1987 (86%).

Of the women in the 1984 survey, 15% reported a health problem, 8% reported mental or emotional problems, 14% of the 2130 who reported live births noted at least one birth defect among their children. Thirty percent of the women reported pregnancies that ended in miscarriage, stillbirth, or abortion. Comparing the specific health problems of the women veterans to a sample of women from another health survey, the only major difference between the two groups of women was a reported rate of cancer almost twice among women veterans as nonveteran women, 8.6% vs 4.8%. The most common cancers among the women veterans were cancer of the uterus, ovaries, or cervix (43%), and breast cancer (26%) (72).

1991 Annual Report of the Secretary of Veterans Affairs

Based on data from the 1991 Annual Report (74), as of September 30, 1991, there were 26.6 million veterans in the United States, of which 1.2 million were women. The median age of all veterans was 55.7 years, with those aged 45 to 64 comprising the largest age group (43%). The median age of women veterans was 49.2 years.

Additional data in the 1991 report included diagnostic data for any veteran discharged from a VA medical center during the fiscal year 1991 (Table 2). These diagnostic data were based on the computerized discharge records of all VA medical centers (Patient Treatment File). During the fiscal year
Table 2  Selected diagnoses* for veterans discharged from VA hospitals

<table>
<thead>
<tr>
<th>Diagnostic Groupb</th>
<th>Under 35 %</th>
<th>35–44 %</th>
<th>45–54 %</th>
<th>55–64 %</th>
<th>65–74 %</th>
<th>75–84 %</th>
<th>85–+ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious diseases (000–139)</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Neoplasms (140–23)</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>12</td>
<td>13</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Blood and blood organ diseases (280–289)</td>
<td>.6</td>
<td>.5</td>
<td>.6</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mental disorders (291–319)</td>
<td>58</td>
<td>57</td>
<td>33</td>
<td>12</td>
<td>7</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Nervous system diseases (320–389)</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Circulatory diseases (390–458)</td>
<td>2</td>
<td>5</td>
<td>14</td>
<td>21</td>
<td>22</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>Respiratory diseases (460–519)</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Injury and poisoning (E800–E999)</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

*Based on 944,162 principal diagnoses for veterans discharged from VA medical centers, fiscal year 1991, as recorded in the Patient Treatment File.

1991 there were 944,162 discharges of veterans from VA medical centers, with the largest percentage of hospital discharges accounted for by those aged 65–74 (31%), followed by those aged 55–64 (24%). The lowest number of hospital discharges was among those younger than 35 (6%) and 85 or older (1%). As expected, the percentage of veterans treated for diseases related to age, e.g. circulatory diseases, respiratory diseases, and cancer, increased with age. A large number of veterans age 44 or younger were treated for mental disorders (57%). The percentage of diagnoses related to mental disorders dropped significantly as age increased. The most common mental disorder diagnosis was alcohol and drug dependence. The surveys indicate that the composition of the veteran population is changing, and therefore veteran needs and issues are also changing. The survey data are limited by the self-reported nature of medical conditions, and the hospital data are subject to self-selection bias. However, the usefulness of these data in allocating VA resources is without question.

Specific veteran health issues vary according to the period of military service. The effects of mustard gas are of concern for WWI and WWII veterans, and the effects of ionizing radiation for post-WWII veterans who participated in atmospheric nuclear tests. Agent Orange exposure and Post Traumatic Stress...
Disorder (PTSD) are the significant health issues for Vietnam veterans, whereas the effects of exposure to pollutants from oil fires and other chemicals are troubling to veterans who served in the Persian Gulf.

SPECIAL VETERAN POPULATIONS

WWII Veterans Exposed to Mustard Gas

Mustard gas, a chemical vesicant, was first used in warfare by the Germans in 1917, against British troops. During WWI as many as 28,000 of the American Expeditionary Forces suffered casualties from exposure on the battlefield. Soldiers were seldom exposed to lethal concentrations of mustard gas because of dispersion of the gas in the battlefield. During WWI, soldiers exposed to mustard gas first experienced irritation of the nose causing sneezing, followed a few hours later by signs of mustard gas poisoning: inflammation of the eyes and vomiting, followed by erythema of the skin and blistering. By the time the soldiers reached the casualty clearing stations they were virtually blind. Death within 24 hours usually resulted from chemical pneumonia, and after 24 hours from bacterial pneumonia. Most of the mustard gas casualties evacuated to England suffered from bronchitis, bronchopneumonia, burns, severe conjunctivitis, and various types of heart conditions. Sixty to 70 percent of all cases treated for mustard gas poisoning recovered within six weeks, and within two months all but a small number of severely affected persons had returned to duty.

Although mustard gas was not used in World War II, the Germans, Japanese, Americans, and British produced and stockpiled the chemical for possible use. At the beginning of the war, the US military initiated a secret research program to prepare against the threat of chemical attack by Germany or Japan. As no effective protection against the vesicant was known, top secret experiments of protective equipment, clothing, and antivesicant ointments were conducted at several sites, using military volunteers.

Three basic types of experiments were conducted with soldiers and sailors, of which the most common were patch or drop tests to assess the efficacy of protective ointments. A small amount of liquid mustard was applied on the forearm before or after application of some test ointments. At least 15,000 and perhaps as many as 60,000 WWII veterans were reported as having participated in these tests. In chamber tests, human volunteers wearing protective masks and clothing were each exposed to mustard gas in a gas chamber for an hour or more everyday or every other day until their skin showed evidence of moderate to intense chemical burns (erythema). The skin reaction would indicate that mustard gas was penetrating the protective mask or clothing.
Field tests required soldiers to traverse tropical or subtropical terrains where mustard gas was dropped to determine the value of masks, protective clothing, and ointments. Penetration of mustard gas through the protective equipment was also assessed by evidence of skin damage. At least 4000 US servicemen participated in the chamber tests or in field exercises over contaminated ground areas. No central roster was compiled of military personnel who volunteered for the testing programs, so the actual number and identity of all of the veterans exposed to vesicant are yet to be determined. Many WWII veterans have contacted the US Department of Veterans Affairs about health problems that they attribute to their exposure to mustard gas.

Late effects of exposure to mustard gas have been studied in British and US veterans of WWI and in workers involved with manufacture of mustard gas during WWII. A British study compared the mortality records from 1930 to 1952: 1267 war pensioners who suffered from mustard gas poisoning during WWI with those of two other groups: 1421 war pensioners who suffered from chronic bronchitis and 1114 war pensioners who were wounded but had not been poisoned by mustard gas (16). Mortality from cancer of the lung and pleura and chronic bronchitis was significantly higher among the mustard gas group and the chronic bronchitis group. A US study followed the mortality patterns from 1919 to 1955 (6) of 2718 veterans exposed to mustard gas, 1855 veterans who had pneumonia during the 1918 influenza epidemic but who had not been exposed to mustard gas, and 2578 wounded veterans with no history of mustard gas exposure or of pneumonia. The author concluded that the evidence was suggestive of increased lung cancer in veterans who had been subjected to mustard gas poisoning in 1918. An additional 10 years of follow-up of these veterans did not change the original conclusion (56).

A stronger association between mustard gas exposure and respiratory cancer is shown in the studies of workers exposed to mustard gas during the manufacture of the chemical. A mortality study of 3530 men and women employed in a British factory that manufactured mustard gas during WWII showed highly significant excesses of deaths from cancer of the larynx, pharynx, and other upper respiratory sites when compared to the national population. For lung cancer, the excess was also significant but moderate. Dose-response relationships, where dose was measured by duration of employment, were observed for cancers of the lung, pharynx, and larynx (26).

The literature suggests that the long-term effects of both WWI battlefield exposure (acute exposure) and occupational exposure (chronic exposure) to mustard gas may include the increased risk of respiratory cancer and nonmalignant respiratory diseases (pneumonia, bronchitis). However, there
are few directly relevant data for evaluating the risk of the late effects of mustard gas associated with the specific exposure conditions experienced by the WWII test participants. Studies of WWI veterans are suggestive of an increased risk of respiratory cancer, but almost all men exposed to mustard gas also experienced acute pulmonary reactions. Whether long-term health effects of exposure to mustard gas can occur among WWII veterans in the absence of initial acute injury to the respiratory tract and skin needs to be studied. A significant number of WWII veterans were exposed to mustard gas during military experiments, and approximately two thirds of them should be still alive. Their exposure almost 50 years ago provides a sufficient latency period for chemically induced malignancy.

One of the most challenging aspects of studying the WWII veterans who volunteered for the testings is the identification of these veterans. Because of the secrecy surrounding the testing program, records of their participation are not readily available to the public. VA is working closely with the Defense Department to identify the test participants. Once the roster of participants is assembled and verified, mortality and morbidity studies can be undertaken to evaluate the long-term effects of mustard gas on these veterans.

**Post-WWII Veterans Who Participated in Nuclear Weapon Testing**

The United States conducted the first atomic bomb detonation on July 16, 1945, in New Mexico. From 1945 through 1962, the Manhattan Engineer District and its successor agency, the Atomic Energy Commission, conducted 235 atmospheric nuclear tests, primarily in Nevada and the Pacific Ocean. The Department of Defense estimated that approximately 250,000 military personnel participated in the tests. An additional 190,000 soldiers were potentially exposed to ionizing radiation as occupational forces within 10 miles of the city limits of either Hiroshima or Nagasaki, Japan, both sites of atomic bombing in August, 1945. Many American prisoners of war were also interned within 10 miles of the city limits at the time of the nuclear bomb detonation.

Some test participants were exposed to initial radiation emitted from the fireball and the cloud column during the first minute after the detonation. Others were exposed to residual radiation from military operations in a contaminated environment resulting in inhalation or ingestion of radioactive materials. When the first US occupation forces entered Hiroshima two months after the detonation, the intensity of induced radioactivity around the hypocenter was 0.03 milliroentgen per hour, which was reported to be a negligible level of radioactivity. About the same levels of induced radioactivity remained in Nagasaki when the main body of US troops arrived
45 days after the bombing (71). Many of the 250,000 test participants were exposed to low levels of radiation. The overall average radiation dose was estimated as 0.6 rem per year. Approximately 1700 personnel exceeded the current Federal Occupational radiation exposure guideline of 5 rem per year.

The biological effects resulting from exposure to ionizing radiation have been closely studied and are well documented. Examples of acute effects are erythema, blood changes, vomiting, loss of hair, and even death. Observable acute effects seldom occur at radiation doses below approximately 25 rem. Examples of delayed effects include cataracts and several forms of cancer. No threshold dose is required for induction of radiogenic cancer. Among atomic bomb survivors of the Hiroshima and Nagasaki attack leukemia, cancer of the thyroid, lung, stomach, colon, and esophagus were reported in excess (54).

In 1976, a claim relating acute myelocytic leukemia to radiation exposure from nuclear weapon testing received extensive publicity. This case prompted the Center for Disease Control (CDC) to study the incidence of leukemia among the veterans who participated in Shot Smoky (13), a 44-kiloton detonation that took place in August, 1957, as part of Operation Plumbob. Nine leukemia cases were identified among 3224 veterans, whereas 3.5 leukemia cases would be expected based on age- and sex-specific leukemia incidence rates in the general population. The CDC concluded that if the apparent excess of leukemia were not a chance occurrence, the Smoky participants may have received higher than anticipated radiation doses (perhaps from neutrons or inhaled radioactive material not detected by film badges), or radiation is more carcinogenic at low doses than previously assumed. This report generated considerable interest and prompted a follow-up study of the incidence as well as mortality rates of all forms of cancer (12). A total of 112 cancer cases were identified, which is below the expected number of 117.5 cases. Cancers of the digestive system, respiratory, genital, and urinary system occurred less often than expected. No cancers of the bone, soft tissue, endocrine system, or multiple myeloma were found. Leukemia cases were still significantly in excess among the Smoky participants. The authors concluded that the findings on leukemia were attributable to chance, to factors other than radiation, or to some combination of risk factors that might include radiation, in view of the lack of significant increase in either the incidence of or mortality from any other radiogenic cancers and the apparent lack of a dose effect by units.

The two CDC studies prompted another study by the National Academy of Science (NAS) Medical Follow-up Agency to determine whether the findings from the Smoky participants were unique to that test (59). Five test series were selected, three from the Pacific (Greenhouse, 1951; Castle, 1954; Redwing, 1956) and two from the Nevada Test Site (Upshot Knothole,
Nearly 50,000 participants were identified by March, 1983. Radiation doses could be determined only for two thirds of the participants. The mean radiation dose was estimated to be 0.9 rem with about 2% of participants receiving more than 5 rem. The excess leukemia among Smoky participants was confirmed but no increase in mortality from other forms of cancer was discerned. No evidence was found of increased mortality from leukemia among participants at Plumbob tests or at four other test series. Combined data for the men in all test series showed no excess in deaths due to leukemia (56 observed, 56.4 expected) and a sizable deficit of deaths from all forms of cancer relative to overall mortality rates in the U.S.

The NAS study has been criticized for inappropriate statistical analysis that led to negative conclusions (8). The critics contended that the test participants should not have been compared to the general population because of “the healthy soldier bias”. The military population consisted entirely of persons who were in apparently good health at the time of entry into the service, whereas the general population included those who were sick as well. Three other errors were listed: no analysis of a subgroup of veterans exposed to a higher level of radiation; no analysis of mortality data by latency period; and the combination of radiogenic and nonradiogenic cancers into one category. For example, the NAS analysis combined nonlymphatic leukemias, which are often radiogenic, with lymphatic leukemia, which is not. Correcting for the healthy soldier bias by comparing the standardized mortality ratios (SMR’s) for cancer among Smoky participants with estimated exposure level above 300 mrem to those less than 300 mrem revealed a significant excess in respiratory cancer, leukemia, and all cancer (8). The authors of the NAS study, however, disagreed with the analytical steps suggested by the critics on the grounds that the data were being gerrymandered to make them appear to support preconceived ideas (42).

This much debated study will be repeated by the NAS Medical Follow-up Agency with a necessary modification. Further work by the Department of Defense indicated that about 15,000 of the original study cohort of 50,000 were not actually present at the test sites and that another group of about 28,000 participants was never considered. The updated study will make appropriate adjustments to reconstitute a study cohort and also create a veteran control group of equal size to that of the study cohort. The Medical Follow-up Agency is also conducting a study of the mortality experience of veterans who participated in Operation Crossroads, a nuclear weapon test conducted at Bikini Atoll in July 1946. This study was prompted by concerns on the part of Congress and veterans that participants may have been exposed to ionizing radiation in sufficient amounts to induce cancer. Approximately 46,000 veterans were identified as participants and an equal number of
veterans who were in service at the time but did not participate in the test were selected for a comparison group (41a).

Several thousand "atomic veterans" have sought medical care and compensation from VA for medical conditions that they believe are related to the nuclear weapon testing or to their participation in military operations in or near Hiroshima and Nagasaki. The NAS Committee on the Biological Effects of Ionizing Radiation in 1990 (BEIR V report) (54) determined that lifetime risk of cancer attributable to a given dose of radiation appears somewhat larger than formerly estimated in 1980 (BEIR III report) (54a) for reasons including the following findings. Reassessment of atomic bomb dosimetry at Hiroshima and Nagasaki disclosed that the average dose equivalent in each city was smaller than previously estimated. Furthermore, continued follow-up of the A-Bomb survivors also indicated that the number of excess cancers per unit dose induced by radiation increases with age. The cancer risk estimates reported in the BEIR V report are about three times larger for solid cancers and about four times larger for leukemia than the risk estimates presented in the BEIR III report. The BEIR V report now projects that exposure to an acute whole-body dose of 0.1 Sv (10 rem) to 100,000 males of all ages will result in an additional 500 to 1200 cancer deaths attributable to the exposure.

Further epidemiologic studies of veterans who participated in the nuclear weapon testing and in occupation of Hiroshima and Nagasaki are needed because of the large number of veterans with potential exposure to radiation and because of the uncertainty in how the exposure dose was reconstructed. If the studies show that the rates of cancer mortality in the veteran population in question are similar to those of other veterans who did not participate in the nuclear weapon tests, it may reassure the veterans that they are not at additional risk of cancer. Alternatively, if the studies find an excess in cancer deaths, it may indicate either that the exposure levels estimated by the military were erroneous or that the generally accepted estimates of cancer risk per unit exposure have been grossly underestimated.

Vietnam Veterans Exposed to Herbicides

Of the veteran groups whose service has raised questions concerning possible long-term adverse health consequences, those who served in Vietnam have perhaps generated the most controversy and intense scientific inquiry. Between January 1965 and March 1973, 2.5 to 3 million American military personnel were stationed in Southeast Asia, most of whom served in South Vietnam (75). Contained in the arsenal of US forces in Vietnam were a variety of herbicides used for strategic purposes to defoliate areas of dense jungle. From 1962 to 1971, 75 million liters of herbicides, including over 41 million liters of the phenoxy herbicide Agent Orange, were sprayed on
almost 9% of Vietnam (22). US Air Force personnel sprayed hundreds of acres with Agent Orange, using fixed-wing aircraft as part of Operation Ranch Hand. Spraying on a smaller scale also occurred around American installations, such as base camps and air fields.

Agent Orange is a mixture of the chemical compounds, 2,4-D and 2,4,5-T. The compound 2,4,5-T was contaminated with small amounts of dioxin, a toxicant that is both teratogenic and carcinogenic in animals (45, 55, 58). Some studies of nonveteran groups who have been exposed to phenoxy herbicides in farming or manufacturing have reported increased risk of soft tissue sarcoma and non-Hodgkin’s lymphoma (NHL) (29, 33, 37–39, 41).

The increased risk for some cancers associated with exposure to phenoxy herbicides that was documented in these occupational studies aroused widespread concern about the long-term health of Vietnam veterans. Responding to this concern, research was conducted to determine the effect(s), if any, of Vietnam service in general, or Agent Orange exposure in particular, on the health of Vietnam veterans. The mortality rate of various groups of Vietnam veterans was compared to that of veterans who served during the Vietnam War but not in Vietnam, or to the US general population. Several studies found no excess in either deaths due to all cancers or deaths due to any specific cancer among Vietnam veterans (2, 11, 21, 31, 49). In contrast, other mortality studies reported significant excesses in deaths due to soft-tissue sarcoma (STS) (46), laryngeal cancer (77), Hodgkin’s disease, and testicular cancer (3) associated with Vietnam service. However, the mortality studies looked only at the effects of Vietnam service and not of exposure to Agent Orange.

Many case-control studies have been conducted to determine the association of various cancers with military service in Vietnam. No convincing evidence has been presented of an association between Vietnam service and STS (43, 66), Hodgkin’s disease (67), liver cancer (67), or nasopharyngeal cancer (67). For NHL, the results were not consistent. The CDC reported an excess NHL risk among sea-based blue water Navy Vietnam veterans (65). The risk was not associated with surrogate measures of Agent Orange exposure such as dates of service, type of military unit, and place of employment. A VA study also failed to find an association between NHL and surrogate measures of Agent Orange exposure such as service in specific military branch, in certain areas within Vietnam, or in combat role (23). Although Vietnam veterans tend to report more health problems and symptoms than non-Vietnam veterans, medical examination revealed no significant difference in prevalence of a wide variety of medical conditions and laboratory values between two cohorts (18).

Several studies have directly addressed the issue of Agent Orange expo-
sure. Two studies used potential biological markers to indicate Agent Orange exposure among two groups of Vietnam veterans as evidenced by elevated concentration of dioxin (20, 44). One study compared the dioxin concentration in the adipose tissue of Vietnam veterans to that of Vietnam era veterans and of a group of civilians (44). The other study compared the dioxin concentration in the blood serum of Vietnam veterans to that found in a group of Vietnam era veterans (20). In neither study was an association found between Vietnam service and amount of dioxin in the body. This finding suggests that heavy exposure to Agent Orange was unlikely for most troops. These studies also used surrogate measures of Agent Orange exposure, based on the location of each individual veteran’s unit in relation to an area sprayed with Agent Orange and time lapsed since that area was sprayed. The information relating to areas sprayed with Agent Orange in Vietnam is stored on two computer tapes compiled by the Department of Defense and the US Army and Joint Services Environmental Support Group (69a). In neither study was the likelihood of Agent Orange exposure (as approximated by serving in a sprayed area) associated with elevated concentrations of dioxin.

Some studies have selected groups of veterans presumed to have increased potential for Agent Orange exposure. One such group was made up of Air Force veterans who participated in Operation Ranch Hand (50) and were exposed to the various herbicides used during flight operations as well as during maintenance of aircraft and spraying equipment. The study compared the health outcomes of approximately 1200 Ranch Hand Air Force veterans to those of 19,000 Air Force veterans involved in cargo flights in Southeast Asia. Another study compared the mortality of nearly 1000 veterans who served in the Army Chemical Corps in Vietnam to that of the total US population (68). Among the duties for veterans in this unit were the mixing and application of herbicides including Agent Orange. Neither study documented an excess of deaths due to cancer (50, 68).

Women veterans who served in Vietnam are also of interest. To date only one study has been published examining the mortality of women Vietnam veterans (69). The mortality of approximately 4600 women Vietnam veterans was compared to that of 5300 women veterans who did not serve in Vietnam. The only cause of death found to be significantly elevated among the women Vietnam veterans was death due to motor vehicle accidents. However, among nurses, cancers of the pancreas and uterine corpus were significantly elevated.

Although findings from the various mortality studies have been inconsistent regarding cancer outcomes, they have produced more consistent findings regarding external causes of death. Of those mortality studies previously discussed, six reported statistically significant excesses of deaths due to
external causes (2, 11, 21, 31, 49, 77), which included accidental poisonings, and motor vehicle accidents.

The possibility of fathering a child with birth defects as a result of exposure to Agent Orange has been one of the major concerns of Vietnam veterans. There have been numerous instances when Vietnam veterans reported fathering children with congenital malformations. However, little or no evidence supports an association between military service in Vietnam and the risk of fathering children with birth defects (19, 24, 28).

**Vietnam Veterans and PTSD** Another area of concern regarding possible adverse health consequences of Vietnam service is related to mental/psychological health. Much of this research has centered on problems experienced by Vietnam veterans as they adjusted to civilian life (14, 27, 32, 78). Researchers and mental health clinicians have often associated adjustment problems with the occurrence of PTSD among Vietnam veterans. The diagnosis of PTSD is based on a variety of criteria as set forth by the American Psychiatric Association in the Diagnostic and Statistical Manual of Mental Disorders (DSM III-R) (1). One criterion for PTSD is exposure to a traumatic event. Studies of PTSD among Vietnam veterans have reported that seeing comrades killed, being fired upon, and being wounded are all risk factors for PTSD among Vietnam veterans (10, 15, 34, 36, 64). Other studies suggest that experiences prior to military service are responsible for the maladjustment problems of some Vietnam veterans (53, 79). However, these studies did not assess combat exposure nor was PTSD specifically examined as an outcome variable. Estimates of the prevalence rate of PTSD among Vietnam veterans range from 2% to 15% among all Vietnam veterans (17, 47) and 20% to 32% among wounded Vietnam veterans (40, 57).

The excess mortality due to external causes among Vietnam veterans and the high prevalence of PTSD among Vietnam veterans (2, 11, 21, 31, 40, 47, 49, 57, 77), while usually not associated with each other in their respective studies, may actually be related. Like PTSD, suicide has been associated with exposure to a traumatic event (5, 30, 52). Both PTSD and suicide also share certain emotional and behavioral characteristics including withdrawal, social isolation (1, 4, 7, 25, 60, 62), and alcohol and drug abuse (4, 7, 15, 17, 25, 60, 62). To date only one study has examined these two health outcomes for an association between PTSD and traumatic causes of death among Vietnam veterans (9). The findings from this study indicated that PTSD was a statistically significant risk factor for all external causes of death, including accidental deaths, all accidental poisonings, and suicides.

Reviewed collectively, findings from studies of Vietnam veterans do not indicate that Vietnam veterans are dying at a greater rate than other veterans
or the general population except for traumatic deaths. A few studies have reported increased risks for certain types of cancer among Vietnam veterans, but the results are not conclusive. The prevalence rates of PTSD and psychological disorders are consistently high among Vietnam veterans, especially among combat veterans. The studies of reproductive outcomes among male veterans were not associated with the risk of fathering a child with birth defects, spontaneous abortions, still births, or neonatal deaths. Because maternal, not paternal, exposure to dioxin causes adverse reproductive events in animals, a study of women Vietnam veterans for adverse reproductive outcomes is warranted.

**Persian Gulf War Veterans Exposed to Kuwaiti Oil-Well Fires**

On February 15, 1991, the retreating Iraqi Army began destroying and setting fire to oil wells, storage tanks, and refineries in several oil fields in Kuwait. A total of 749 facilities were either set on fire or turned to oil gushers. According to Kuwaiti oil industry officials, up to 6 million barrels of oil were burned each day from 600 oil wells, creating one of the most extraordinary manmade environmental disasters in history. The 600,000 US troops deployed in the region were potentially exposed to smoke and other toxic combustion products. Air pollutants such as hydrogen sulfide, sulfur dioxide, hydrocarbons, particulate matters singularly or in combination can cause acute as well as chronic health problems. Therefore, immediate and long-term health risk to the troops has been of concern to individuals deployed in the region and to government agencies.

Soon after their return from deployment to the Persian Gulf region many soldiers started reporting a wide variety of nonspecific symptoms, including fatigue, joint pains, skin rashes, headaches, loss of memory, diarrhea, bleeding and painful gums, and loss of hair. These soldiers were evaluated by military medical teams without any unifying diagnosis (76). No evidence was reported of an outbreak or cluster of any unique disease process among these soldiers. Dental examination revealed gingivitis, periodontal diseases, caries, and other chronic oral conditions as likely causes for the dental symptoms. Results of specific testing indicated no role for leishmaniasis, brucellosis, and other infectious agents in causing the symptoms reported by this group of soldiers. As of May 1993, only 30 cases of leishmaniasis, a parasitic disease endemic in the Persian Gulf area, had been reported from the entire group of troops deployed in the Persian Gulf.

Stress associated with post-deployment adjustment to civilian life has been suggested as a plausible etiology for many of the symptoms reported (76). In one survey, 22% of 715 troops deployed to the Persian Gulf region reported at least mild levels of clinical depression, whereas 11% of 169...
nondeployed troops had a similar level of depression. The prevalence of PTSD among Gulf veterans was about 10% using the DSM-R-derived PTSD Symptoms Checklist (35).

An alternate etiology proposed for the “mystery illnesses” among Gulf War veterans is multiple chemical sensitivity (MCS) (51). Multiple chemical sensitivity appears to involve two steps: induction or sensitization, and triggering. Induction or sensitization may have occurred among the Gulf veterans following a single, acute exposure or repeated low-level exposures to any of a wide variety of petrochemical combustion products while deployed in the Persian Gulf region. Once sensitized, exposure to extremely low levels of sensitizing agents or other chemicals could trigger a wide range of symptoms such as memory loss, headaches, weakness, fatigue, and mood changes.

The levels of air quality during the oil well fires have been investigated by a US Interagency Air Assessment Team (48). From March through May 1991 the team sampled air near the burning wells, flew instrumental airplanes into smoke plumes, and sampled the air at various locations in the path of the smoke, including population centers in Kuwait and Saudi Arabia. The air samples were analyzed for volatile organic compounds, polycyclic aromatic hydrocarbons, heavy metals, sulfur dioxide and inorganic acids, hydrogen sulfide, and total nuisance dust. Both hydrogen sulfide and sulfur dioxide were present in concentrations below the EPA limits near the sources of the fire and at locations sampled downwind. The only elevated levels observed in the population areas were for particulate matter. A very high level of fine particulate (PM-10), 8 to 10 times the EPA limit of 50 mg/M³, was observed in Kuwait city and Dhahran, Saudi Arabia. These high readings were considered not unusual for the area, probably due to a combination of blowing dust and sand.

Department of Defense also dispatched its own environmental monitoring team to the area (70). A team of industrial hygienists from the US Army Environmental Hygiene Agency monitored the area from May 5, 1991, until December 3, 1991. At the start of monitoring, 558 wells were still on fire. Data collection continued until all fires were extinguished. Air monitoring stations were set up at four locations in Saudi Arabia and six locations in Kuwait, where large numbers of US troops were stationed. Soil samples were also taken to evaluate alternate exposure pathways. The DOD team reported that air sample measurements collected during this period did not suggest the oil fires were significantly contributing to air quality at ground-level sampling sites. Mean concentrations of organic compounds measured in Kuwaiti and Saudi sampling sites were comparable to levels observed in US cities (Houston, Philadelphia). In most cases concentrations of polycyclic aromatic hydrocarbons were below the detection levels. High concentrations
of particulate matter were measured at all sampling locations as reported by the interagency team.

VA has initiated a health registry in response to health concerns expressed by the Persian Gulf War veterans. All Persian Gulf veterans with medical concerns that they believe are related to their deployment in the Persian Gulf region, are encouraged to come to a VA medical center for a free physical examination. Their demographic and medical data are included in the registry.

Demographic characteristics from the Registry for the first 1404 registry participants nearly approximate the characteristics of troops deployed in the area. Symptoms reported by the registry participants were nonspecific and were similar to complaints reported by other groups of Persian Gulf veterans. The common complaints were fatigue, skin rash, headache, loss of memory, muscle/joint pain, shortness of breath, cough, diarrhea, and chest pain. A wide range of medical conditions were diagnosed among the participants. About 20% of participants did not have a medical diagnosis. Prevalence of chronic respiratory diseases did not seem to be unusually high among these veterans: chronic bronchitis (1.2%), asthma (3.7%), chronic airway obstruction (1.9%). Prevalence of chronic PTSD was lower than reported in other groups of Persian Gulf veterans (2.6% observed vs 10% reported in another survey). Veterans with symptoms or with medical diagnoses were more likely to report having been in the contaminated area, in a smoky area, enveloped in smoke, or eating/drinking contaminated foodstuff than veterans without symptoms or medical diagnoses (74a).

Veterans in the Persian Gulf Registry, like those in the Agent Orange Registry, are self-selected for their concern about the possible adverse health effects from environmental conditions experienced during the deployment and are also willing to visit VA medical facilities for physical examination. Therefore, they may not be representative of the general Persian Gulf veteran population. A valid comparison of health outcomes from this group to another population is difficult to make due to this self-selection bias.

Hospital discharge diagnoses of 4514 Persian Gulf veterans and 4325 era veteran patients in VA medical centers showed no significant difference in distribution of major categories of diagnoses except in the category of adjustment disorders, including PTSD. More than 25,000 Persian Gulf veterans have visited VA's readjustment counseling centers. While there was considerable variation among counseling centers, aggregated data suggest that 9 percent of returning Persian Gulf veterans may have been suffering from significant symptoms of clinical PTSD shortly after their return from the Persian Gulf region.

The study of Persian Gulf War veterans has benefitted from earlier veteran studies, in particular those related to Vietnam. Two major difficulties in
research concerning health effects of Agent Orange have been the inability
to identify a large number of Vietnam veterans who were exposed to Agent
Orange and the uncertainty in assessing the magnitude of their exposure.
Reconstructing the Vietnam data related to Agent Orange after the fact is
extremely difficult. To avoid similar problems in studying Persian Gulf
Veterans, the Department of Veterans Affairs and the Department of Defense
are collaborating to establish the following databases: (a) a roster of troops
assigned to each military unit that served in the Persian Gulf area; (b) a
file of unit location for the period January 15, 1991, through the date of
unit withdrawal from the area; and (c) data on air pollution levels from a
number of locations where troops were deployed. Once the roster of Persian
Gulf-deployed troops is established, a sample of troops on the roster can
be selected to conduct a morbidity or mortality study to test specific
hypotheses about exposure and outcome association.

SUMMARY

Late effects of exposure to certain environmental hazards as a consequence
of their active military service have become an issue of particular concern
to veterans and the public at large. Approximately one out of four Americans
is a veteran or a family member of a veteran. The US military develops
and uses increasingly complex and sophisticated weaponry. As the military
technology changes, so do the kinds of health issues to be addressed. The
changing composition of military personnel, most notably the increasing
number of women veterans and their expanding role into combat-related
activities, will affect both the health issues to be addressed and the kind
of health care to be provided. The emerging role of the military as
peace-keepers in hostile but nonwar zones and as disaster-relief workers,
often in developing countries, may subject soldiers to infectious diseases
demic to the area and to psychological stressors unrelated to combat.

The formation of a registry of military personnel exposed to potentially
serious long-term health hazards would be highly advisable, whenever
feasible. Such an exposure registry could serve as the basis for future
medical surveillance and response to affected veterans and help avoid the
kind of difficulty experienced in addressing health concerns of WWII
veterans exposed to mustard gas and Vietnam veterans exposed to Agent
Orange. Close cooperation between the Department of Veterans Affairs and
the Department of Defense is essential in the identification of potential
hazards and follow-up of affected individuals. Growing public awareness
of potential occupational and environmental hazards, publicity surrounding
such suspected health risks, and the limited scientific knowledge about
low-level exposure to toxic substances may all lead to misunderstanding,
unwarranted fear, and suspicion of government coverup. Establishment of an exposure registry of veterans may be seen as a government commitment to address the future effects of potential hazards.

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Literature Cited

22. Comm. on the Effects of Herbicides in Vietnam. 1974. The effects of her-
88 BULLMAN & KANG


HEALTH RISK ASSESSMENT OF VETERANS