Surveillance of Health Outcomes of Gulf War Veterans

Han K. Kang, Dr.P.H.
Director
Environmental Epidemiology Service &
War-Related Illness and Injury Study Center
Washington DC VA Medical Center

Gulf War Advisory Committee Meeting
Washington, DC November 20, 2008
### Key Dates During Operations Desert Shield/Desert Storm

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td></td>
</tr>
<tr>
<td>August 2</td>
<td>Iraq invaded Kuwait</td>
</tr>
<tr>
<td>August 8</td>
<td>U.S. Air Force planes arrived in Saudi Arabia</td>
</tr>
<tr>
<td>August 9</td>
<td>U.S. ground forces arrived in Saudi Arabia</td>
</tr>
<tr>
<td>November 8</td>
<td>President Bush orders an additional 150-200,000 (400,000 total)</td>
</tr>
<tr>
<td>November 29</td>
<td>UN resolution authorizing use of “all necessary means”</td>
</tr>
<tr>
<td>1991</td>
<td></td>
</tr>
<tr>
<td>January 17</td>
<td>First irretrievable hostile fire</td>
</tr>
<tr>
<td>January 20</td>
<td>First oil well fires started in Kuwait</td>
</tr>
<tr>
<td>February 19</td>
<td>Majority of oil well fires ignited</td>
</tr>
<tr>
<td>February 24</td>
<td>Ground war began</td>
</tr>
<tr>
<td>February 28</td>
<td>Offensive operations ceased</td>
</tr>
<tr>
<td>March 4,10</td>
<td>Khamisiyah, Iraq chemical munitions destruction</td>
</tr>
<tr>
<td>June 13</td>
<td>Last U.S. service members who participated in the ground war returned to the United States</td>
</tr>
</tbody>
</table>

(Source: Presidential Advisory Committee on Gulf War Veterans’ Illnesses, 1996)
Number of U.S. Troops in the Persian Gulf Theater of Operations by Month

(SOURCE: Information provided by the Defense Manpower Data Center (DMDC))
Demographic and Military Characteristics of 695,516 Gulf War Veterans

(SOURCE: Kang and Bullman, NEJM 1996;335:498-504)
## Percent Distribution of Potential Exposures of Concern Reported by Gulf War Veterans

<table>
<thead>
<tr>
<th>Exposure of Concern</th>
<th>National Survey (N=11,441)</th>
<th>VA Registry (N=15,891)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petrochemical fumes (including tent heater, vehicle exhaust)</td>
<td>80.4</td>
<td>90.3</td>
</tr>
<tr>
<td>Ate local food</td>
<td>74.9</td>
<td>70.7</td>
</tr>
<tr>
<td>Wore chemical protective gear (other than training or heard chemical alarms sound)</td>
<td>65.5</td>
<td>66.6</td>
</tr>
<tr>
<td>Smoke from oil well fires</td>
<td>65.1</td>
<td>72.8</td>
</tr>
<tr>
<td>Burning trash/feces</td>
<td>60.0</td>
<td>74.7</td>
</tr>
<tr>
<td>Skin exposure to diesel, other petrochemical</td>
<td>56.6</td>
<td>73.9</td>
</tr>
<tr>
<td>Personal pesticides (creams, sprays, other)</td>
<td>48.4</td>
<td>67.2</td>
</tr>
<tr>
<td>SCUD missile explosion</td>
<td>43.2</td>
<td>-</td>
</tr>
<tr>
<td>Contact with prisoners of war</td>
<td>32.8</td>
<td>-</td>
</tr>
<tr>
<td>Dead animals</td>
<td>32.2</td>
<td>-</td>
</tr>
<tr>
<td>Ate food contaminated with smoke, oil, other chemicals</td>
<td>30.2</td>
<td>33.9</td>
</tr>
<tr>
<td>Other paint and/or solvent and/or petrochemicals</td>
<td>29.7</td>
<td>53.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure of Concern</th>
<th>National Survey (N=11,441)</th>
<th>VA Registry (N=15,891)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bathed in or drank water contaminated with</td>
<td>28.1</td>
<td>29.3</td>
</tr>
<tr>
<td>smoke, oil, other chemicals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Involved in direct combat duty</td>
<td>27.2</td>
<td>29.9</td>
</tr>
<tr>
<td>Witnessed any deaths</td>
<td>26.4</td>
<td>21.7</td>
</tr>
<tr>
<td>Microwaves</td>
<td>23.7</td>
<td>34.2</td>
</tr>
<tr>
<td>Bathed or swam in a local pond, river, or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persian Gulf water</td>
<td>23.3</td>
<td>29.3</td>
</tr>
<tr>
<td>Chemical Agent Resistant Compound paint</td>
<td>21.7</td>
<td>35.0</td>
</tr>
<tr>
<td>Nerve gas</td>
<td>9.6</td>
<td>15.8</td>
</tr>
<tr>
<td>Depleted uranium</td>
<td>9.5</td>
<td>15.1</td>
</tr>
<tr>
<td>Experienced sexual harassment</td>
<td>5.1</td>
<td>-</td>
</tr>
<tr>
<td>Mustard gas or other blistering agents</td>
<td>4.8</td>
<td>7.2</td>
</tr>
<tr>
<td>Suffered forced sexual relations or sexual assault</td>
<td>0.8</td>
<td>-</td>
</tr>
</tbody>
</table>

Health Assessment
Gulf War Era Veterans

Mortality
Gulf: 700,000
Controls: 750,000

VA/DOD USUHS MVA Study

ALS, Brain CA, MS, Parkinson’s

Health Registry
VA PGR: 70,000
DOD CCEP: 30,000

Combined VA/DOD NHRC Registry Analysis

IOM/VA Nerve Gas Exposure Study

GWU/VA Gulf War Syndrome Study

Neuropsychologic Assessment Study

VA/DOD Health Care Utilization
Inpatient
Outpatient

Population - Based Health Survey
N= 30,000

Phase I and II
Mail or CATI Survey
Medical Records Review
N=30,000

Cancer Study State Tumor Registry

Unexplained Illness Study

ALS, Brain CA, MS, Parkinson’s

Phase III Clinical Study
CSP #458
N=5,000

Longitudinal Health Study
N=30,000

Unexplained Illness Autonomic Functions

Excess Fatigue Motor Neuron Function
Gulf War Veterans Mortality

Publications


Mortality Studies Results

1. Overall mortality rate of Gulf War veterans is not higher than non-Gulf veterans.

2. Mortality rates from accidents, especially motor vehicle accident were higher and from disease-related causes were lower among Gulf War veterans than non-Gulf veterans.

3. These differences in mortality patterns began to dissipate after 5 years since the war.

4. Both Gulf and non-Gulf veterans mortality rates remained less than half that expected from their civilian counterparts.

5. Both US and UK study results are remarkably similar.

6. Gulf War veterans who were potentially exposed to nerve agent had an increased risk of brain cancer death compared to other Gulf War veterans.
Suicide Rates among Male Gulf and Non-Gulf Veterans Compared to U.S. Male Suicide Rates, 1991-2004

U.S. male suicide rate from www.cdc.gov/niosh/LTAS
Suicide Rates among Female Gulf and Non-Gulf Veterans Compared to U.S. Female Suicide Rates, 1991-2004

U.S. female suicide rate from www.cdc.gov/niosh/LTAS


MVA Study Findings

1. Veterans who died of MVA were disproportionately younger, less educated, not married, enrolled, and deployed to the Gulf War.

2. Gulf veterans who died of MVA were disproportionately more involved in a single-vehicle crash, alcohol related crashes, and non-users of seat belt.

3. Possible exposure to nerve agents at Khamisiyah was not associated with post war MVC among Gulf veterans.
Gulf War Veterans Health Registry Publications


Registry Studies
Major Findings

• Based on hospitalization data, registry participants sicker than non-participants (Smith, 2004)
• Self reported symptoms: fatigue, headache, memory problems, sleep disturbance, skin rash, joint pain, dyspnea, cough (multiple US and UK studies)
• Registry participants reported high prevalence of GW related exposures (multiple US studies)
• High symptom reporting among registrants associated with belief in chemical or biological warfare exposure, war stressors, & negative life events after the war (Boyd, 2003)
• Most frequently reported disease classifications: mental disorders, respiratory disorders, skin conditions, and musculoskeletal diseases (Gray 1998, 2004; VA 2002)
Registry Studies
Value and Limitations

Value
• Identified those seeking medical evaluation
• Detailed clinical exams
• Helped define unexplained illnesses as symptom-based
• Source for case/control study subjects
• Value in negative findings
  – Did not implicate a specific etiologic exposure
  – Did not support existence of a unique group of symptoms or “Gulf War Syndrome”

Limitations
• Limited research value
• Self selected participants
• Not representative of all deployed personnel
• Motivation for participation varied
  – Illness
  – Possibility of compensation
  – Media influence
• No control population for comparison
Health Care Utilization

Publications


Health Care Utilization Findings

1. No excess postwar hospitalization (1991-1994) due to major categories of diseases in VA, DoD and California hospital system

2. However, a small but significant excesses in hospitalization due to mental disorders, diseases of respiratory system and the digestive system, diseases of skin, and symptoms, signs and ill-defined conditions are observed among Gulf veterans treated at VA hospitals.
Purpose of the National Health Survey

• To estimate and compare prevalence of various symptoms and other health outcomes among Gulf veterans and those of non-Gulf veterans.

• To estimate and compare prevalence of various reproductive outcomes among spouses and birth defects among children of Gulf veterans and those non-Gulf veterans.

• To evaluate the relationship between selected symptoms and health outcomes and certain environmental exposures in the Gulf area.
STUDY SUBJECTS

Population based sample of 15,000 Gulf veterans (DS/DS participants) and an equal number of Gulf-era veterans.
Distribution of Gulf War Veterans and Non-Gulf War Veterans in the survey by Gender and Unit Component

<table>
<thead>
<tr>
<th>Unit Component</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>4,800</td>
<td>1,200</td>
<td>6,000</td>
</tr>
<tr>
<td>Reserve</td>
<td>4,000</td>
<td>1,000</td>
<td>5,000</td>
</tr>
<tr>
<td>National Guard</td>
<td>3,200</td>
<td>800</td>
<td>4,000</td>
</tr>
<tr>
<td>Total</td>
<td>12,000</td>
<td>3,000</td>
<td>15,000</td>
</tr>
</tbody>
</table>
SURVEY DESIGN

• Questionnaires through the mail

• Supplemental telephone interviews

• Physical examinations on a sample of veterans

• Validation through civilian, military and VA medical records
QUESTIONNARE INSTRUMENTS

- Limitations of activities
- Use of medical services (hospitalization, clinic visit)
- Chronic medical conditions (31 items)
- Prevalence of symptoms (48 items)
- Exposures in the Gulf theater (24 items)
- Prophylactics, vaccines (9 items)
- Reproductive health and pregnancy outcomes
  - live birth
  - still birth
  - miscarriage
  - birth defects
  - infant deaths
- Life events (14 items)
- Smoking & drinking histories
- PTSD check list (PCL), 17 items


National Health Survey Phase I and II
Publications


National Health Survey

Phase 1 and II Findings

I. Physical Health

Gulf veterans reported higher prevalence of:

• Functional impairment

• Health care utilization

• A wide variety of symptoms

• Serious chronic health conditions

• Lower perception of general health
II. Psychological Health

• Gulf veterans reported higher prevalence of symptoms endorsing PTSD (PCL-M) and chronic fatigue syndrome (CDC 1994)

• The prevalence of PTSD increased monotonically across 6 levels of deployment-related stress intensity (test of trend, p <0.01)

• Gulf veterans reported higher rate of sexual trauma (harassment/assault) in theater, which in turn was associated with the higher prevalence of PTSD even after adjusting for the combat trauma.
III. Reproductive Health

Gulf veterans reported higher rates of:

- **Miscarriage**
  - Male veterans: OR=1.62; 95% CI=1.32-1.99
  - Female veterans: OR = 1.35; 95% CI =0.97-1.89

- **Birth defects among liveborn infants**
  - Male veterans: OR = 1.78; 95% CI=1.19-2.66
  - Female veterans: OR= 2.80; 95% CI=1.26-6.25
IV. Symptom Cluster

• A cluster of symptoms consistent with neurological impairment were identified by a factor analysis: blurred vision, loss of balance/dizziness, tremors/shaking and speech difficulty

• A clinical evaluation of Gulf veterans with a cluster of neurological symptoms indicated the symptom complex appears to correlate with objective neurological abnormalities including abnormal ENG

• Relatively more symptomatic Gulf veterans were exposed to combat, engaged in military duties in Kuwait and Iraq, and potential nerve gas plume from Khamisiyah incident as determined by the Department of Defense
Clinical Study Publications


Clinical Study Neurologic Findings

• No differences in prevalence of distal symmetric polyneuropathy among Gulf veterans and non-Gulf veterans by electrophysiologic assessment of motor and sensory nerves and by history and physical examinations.

• Of the battery of neurologic tests (ENG, VER, BAER and SSEP), only the ENG supported the validity of the neurologic symptoms reported in the 1995 survey
Neurologic and All Cause Mortality, 13 year Follow-up Results

As of 12/31/2004 among 621,901 Gulf veterans and 746,247 non-Gulf veterans

1. All Causes - Gulf: 10,869 deaths; non-Gulf: 14,716 deaths
2. MVA - Gulf: 1,776; non-Gulf: 1,817
3. Suicide - Gulf: 1,514; non-Gulf: 1,722
4. MS - Gulf: 6; non-Gulf: 13
5. Parkinson’s disease – Gulf 3:; non-Gulf: 8
6. ALS - Gulf: 23; non-Gulf: 38
7. Brain cancer - Gulf: 144; non-Gulf: 228
Summary

The general aims of epidemiologic research are to 1) describe the health status of populations, 2) explain the etiology of diseases, 3) predict and quantify disease occurrence, and 4) control the distributions of diseases in the population.

- Define and characterize population at risk
- Assess potential exposure of concern
- Develop potential health outcomes of interest
- Design a study based on many factors including size of available study group, health outcomes of interest, nature and extent of measurement error

Cohort study vs. Case-control Study
Cross-sectional and other types of studies
Experimental vs. Observational