Appendix B-2

MVHCB Second Annual Plenary Conference December 10-12, 2001

Part Two of Two

IS THERE A GULF WAR SYNDROME? ROUND 3

Simon Wessely

Guy's, King's and St. Thomas' School of Medicine, London, UK

s.wessely@iop.kcl.ac.uk

There is a simple and a complex way to answer this question.

First, the complex one. This involves using multivariate statistics to discover how symptoms in Gulf veterans aggregate together, which they do, and then seeing whether or not a different pattern is observed in appropriate control populations. Four studies, one of which is ours, have tried this, and the answer is no. Hence yes there are Gulf War syndromes, but no, these don't differ from non Gulf War syndromes.

The objections to this approach are

a) All four groups, independently, managed to carefully avoid asking the right symptoms, which would have demonstrated the real Gulf War Syndrome

b) All four groups, independently, managed to use the wrong statistics

To answer those criticisms I shall use common sense and the naked eye.

But this is all very well, but we are missing the point. The question of whether or not there is a Gulf War syndrome is an academic issue that only a handful of statisticians with experience in the minutiae of factor analysis are equipped to answer.

What is important, and can be appreciated without the hinderance of factor analysis, is that there is a Gulf War health effect and it is substantial.

References

Ismail K, Everitt B, Blatchley N, et al. Is there a Gulf war syndrome? Lancet 1999;**353:**179-182.

Everitt B, Ismail K et al. Factor and cluster analytic approaches to the problem of Gulf War ill health. Submitted for publication

APPROACHES TO CASE DEFINITION IN THE IOWA STUDY SYNDROME ANALYSIS

BN Doebbeling[1,2,3], WR Clarke,[4] D Watson,[5] MD Voelker,[2,4] JC Torner[3], and RF Woolson[4]

[1]Veterans' Affairs Medical Center, Iowa City, IA;
[2]Department of Internal Medicine, University of Iowa College of Medicine;
Departments of [3]Epidemiology, and [4]Biostatistics, University of Iowa College of Public Health;
and [5]Department of Psychology, University of Iowa

Introduction

The original Iowa Gulf War Study was initiated to investigate the prevalence of self-reported symptoms and illnesses five years post-conflict among military personnel deployed to the GW theater (GWD), and those activated but not deployed (GWE). Empirical algorithms were defined *a priori* based on case definitions described in the literature to identify individuals with symptoms likely to indicate the presence of specific health outcomes. We reported that GWD had a higher prevalence of symptoms of health outcomes including cognitive dysfunction, depression, post-traumatic stress disorder, chronic fatigue, bronchitis, asthma, fibromyalgia, alcohol abuse, anxiety and sexual discomfort. [*JAMA*, 1997][1] A number of reports clearly document elevated self-reported health problems among Gulf War veterans. Research efforts continue to examine symptomatic veterans and appropriate controls clinically, and to explore and identify risk factors for these health outcomes.

While clinical evaluations have identified medical or psychological conditions among many Gulf War veterans, symptomatology often remains unexplained. There is growing interest in symptom epidemiology, owing to the considerable healthcare demand and functional impairment associated with non-specific symptoms. No discernible cause is found for many of these complaints in the general population. Concerns have been raised that the multiple unexplained symptoms observed in Gulf War veterans signify a unique medical illness or "Gulf War syndrome(s)" etiologically linked to Gulf War military service.

Factor analysis of symptom data from Gulf War veterans has been used to explore this issue. Factor analysis is a useful tool for data reduction and the identification of latent variables. Factor analysis characterizes the covariance among many variables in terms of a few underlying but unobservable quantities, called factors. It is assumed that certain variables correlate because they reflect the influence of the underlying factor. Existence of a factor is inferred from the presence of several intercorrelated variables. Identification of unique symptom patterns or "factors" among GWD may imply a definable disorder or disease for which there is a likely etiology, clinical course and potential treatment. To investigate this, we utilized our population-based survey of military personnel to look for evidence of an illness that was unique to those deployed to the Persian Gulf and was not seen in comparable military controls .[*Am J Med*, 2000] [2]

Hypothesis

The *a priori* assumption was that the symptom structure would vary across the deployed and non-deployed, based on the hypothesized existence of a "Gulf War syndrome." Assuming it represents a novel illness, this syndrome should produce a unique pattern of covariation among its constituent symptoms found only in the deployed. Military personnel not serving in the Gulf War could not experience the symptoms, and should produce a different factor structure. Thus we hypothesized that if a unique illness existed, the symptom pattern in deployed would differ from that found in non-deployed.

Methods

A stratified sample of veterans deployed to the Gulf War (GWD) and Gulf War–era military controls who did not serve in the Gulf (GWE) were surveyed in 1995 to 1996. Importantly, this is one of the few population-based studies to evaluate all service branches, evaluating both those remaining on active duty and those discharged. Study procedures and instruments were approved by the Institutional Review Board and a Public Health Service Certificate of Confidentiality was obtained. The structured telephone interview, conducted by an experienced research group, assessed a broad array of health concerns, symptoms and potential risk factors. The item pool contained multiple medical symptom items related to disorders hypothesized to potentially occur at an increased prevalence among Gulf War veterans as well as symptom items covering all major bodily systems. The symptom items were primarily investigator-derived, based on published peer-reviewed data, interviews with Registry participants, pilot studies, and input from public and scientific advisory committees. Subjects were asked whether any of 78 symptoms had been persistent or recurrent in the past year. If present, they rated how much it bothered them: a little bit, moderately,

quite a bit or extremely, coded from 0 (none) to 4 (extremely). The response format was dichotomous for 35 additional symptom items from standardized instruments and 24 other medical problems. Variables were coded positive if present in the past year and onset was during or after the conflict, otherwise were coded negative. Declined responses were coded as missing and "don't know" responses as negative.

Symptom prevalence rate differences and 95% confidence intervals were calculated. Symptom data were transformed based on the cumulative distribution percentage to ensure that the data were on a comparable scale, normally distributed, and to permit conventional multivariate analysis. Since we were interested in identifying a unique pattern of symptoms found only in the deployed, the two cohorts were examined separately. The resulting factor analytic solutions were compared to determine the extent to which they differed.

A popular and scientifically compelling approach to determine the number of factors to retain is to select the most robust and replicable solution. This approach was adopted, using data from the deployed group to form two randomly selected, approximately equal-sized "derivation" and "validation" subsamples. The results in the derivation sample were compared with those obtained in the validation sample of deployed veterans to determine whether the results were replicable. Factors in each solution were carefully inspected for interpretability and for comparability across the two subsamples. A factor was considered interpretable if it had at least three clear marker variables and was clinically meaningful. Replicability was corroborated by formal quantitative tests of factor agreement. First, the item loadings (i.e., correlation between an observed variable and the factor) on the factor were correlated across the two subsamples. If the same symptom variables have high (or low) loadings on the factor in both solutions, this would yield a very strong positive correlation (convergence) between the two arrays. Second, factor scoring weights were used to compare factor scores across the two subsamples. Factor scoring weights are a set of regression weights generated for each extracted factor, where the factor is the outcome and the variables are the predictors. These weights can be applied to the standardized item responses to yield a score reflecting each subject's estimated position on the underlying dimension. If the factors from two different solutions are very similar, they should generate very similar factor scoring weights--and very similar factor scores. Finally, parallel factor analyses were conducted in the non-deployed to determine the extent to which it yielded a uniquely different structure. The symptom structure in the non-deployed was compared to that of the combined deployed group. To assess factor convergence, factor scores were computed using the factor scoring weights from the overall deployed and non-deployed samples and correlations between the two solutions compared.

Results

Interviews were completed on 3,695 (GWD, n= 1896; GWE, n= 1799) of 4,886 eligible subjects, for a 76% participation rate (91% of located subjects). Participants represented 889 deployed and 893 non-deployed units and experienced a variety of military exposures. One half (50%) of the deployed veterans and 14% of the nondeployed controls attributed health problems to military service between 1990 to 1991. Gulf War deployed veterans had significantly higher prevalence rates than era controls for 123 of 137 (90%) symptoms; none were significantly lower. The greatest symptom rate differences between the deployed and non-deployed included polyarthalgia, fatigue, joint stiffness, headaches, and memory problems.

A full range of factor solutions, starting with one factor and ending with ten factors, was conducted in random samples of the deployed. Varimax (uncorrelated) and promax (correlated) factor rotations yielded similar results, consequently, only the varimax results are reported. Factor analysis identified three symptom factors replicable and interpretable in the deployed subsamples. More differentiated solutions also yielded interpretable factors, but did not replicate well. Factor loadings across the subsamples yielded convergent correlations of .85 or greater, indicating that the same variables defined factors in both subsamples. Additionally, the respective factor score intercorrelations across subsamples were .88 or greater indicating a very high level of replicability. Because this structure was robust across the subsamples, a final 3-factor solution was calculated using the entire deployed sample. This solution was consistent with the subsample analyses. The factors were identified as "Somatic Distress," "Psychological Distress," and "Panic"; accounting for 15%, 15%, and 5% of the variance, respectively. The "Somatic Distress" factor markers included joint stiffness; myalgias; polyarthralgia; numbness or tingling; headaches; and nausea. The "Psychological Distress" factor was defined by such symptoms as feeling nervous; worrying; feeling distant or cut off; depression; and anhedonia. The "Panic" factor was defined by a small number of items related to discrete panic attacks and sympathetic hyperarousal.

Parallel factor analyses in the non-deployed produced a very similar, 3-factor solution -- again consisting of "Somatic Distress," "Psychological Distress," and "Panic." These symptom patterns were virtually identical and highly replicable to that observed in the deployed (factor score convergent correlations of 0.95 to 0.98) and accounted for 13%, 11%, and 5% of the variance, respectively. Thus, contrary to our hypothesis, the deployed and non-deployed independently produced the same factor structure.

Conclusions

A consistently higher prevalence of symptoms was reported by Gulf War veterans, compared to the non-deployed cohort. However, the increased prevalence of nearly every symptom, from all bodily systems, in deployed veterans compared to non-deployed is difficult to explain pathophysiologically as a single condition. Researchers have used factor analysis to characterize the factor structure of symptomatology in Gulf War veterans. Identified groups of symptoms or factors have been interpreted as potential syndromes by some investigators. However, our identification of the same replicable factor analytic results among the deployed and non-deployed suggests the health complaints of Gulf War veterans, although more frequent, are similar to those of the general military population. Most notably, a comparable Gulf War Era control group was a crucial strength of our investigation in order to determine whether the findings were unique to the deployed.

Based on our review of the literature and experience with this investigation, we feel that several methodologic issues need to be dealt with carefully if factor analysis is used to develop an aggregation of symptoms that might potentially represent a new Gulf War Syndrome or Illness. First, it is crucial to include a non-deployed comparable military control group to assess whether the same symptoms are reported by nondeployed personnel in similar patterns of response. Second, it is vital to sample from a population of military personnel, rather than a single unit, in order to support generalizability of the results. Although data from a single unit or cluster sample may help raise hypotheses, it is unlikely to be adequate to test them. Third, a high participation rate in the study is crucial in order to demonstrate that the study participants are representative of the group from which they were selected. Fourth, there needs to be an evidence of replicability, at least within the population sampled, if not within other populations and by other investigators. The proposed case definition needs to be clearly enough described that other investigators can attempt to replicate the findings based on the description of the methods in the peer-reviewed literature. Fifth, if a case-definition is proposed based on a factor analytic aggregation of symptoms, there needs to be an assessment by skilled clinicians in order to confirm that the statistical groupings of symptoms make clinical sense and are not explained by a previously recognized medical condition. To advance science requires independent replication of findings.

Our results do not demonstrate the existence of a unique Gulf War syndrome as the cause for unexplained illness. These results are consistent with three other recent well-designed, population-based studies, each using different populations and methods.[2-5] Our results should help alleviate concern about an unexplained "mystery illness" and lead to the expeditious clinical evaluation and treatment of those who remain symptomatic.

References

1. Doebbeling BN, Clarke WR, Watson D, et al. Is There a Persian Gulf War Syndrome? Evidence from a Large, Population-based Survey of Veterans and Nondeployed Controls. *Am. J. Med.* 108(9):695-704, 2000.
2. The Iowa Persian Gulf Study Group. Self-reported Illness and Health Status among Gulf War Veterans: A Population-Based Study. *JAMA*, 277:238-245, 1997.
3. Fukuda K, Nisenbaum R, Stewart G, et al. Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *JAMA*. 1998;280:981-988.
4. Ismail K, Everitt B, Blatchley N, et al. Is there a Gulf War syndrome? *Lancet*. 1999;353:179-182.
5. Knoke JD, Smith TC, Gray GC, et al. Factor analysis of self-reported symptoms: does it identify a Gulf War Syndrome? *Am J Epidemiol* 2000;152(4):379-88.

This work was partially supported by CDC Cooperative Agreement, U50/CCU711513, Department of Defense Grant #DAMD17-97-1-7355. Dr. Voelker was also supported by NIH training grant # 5 T32 MH15158-23.

FACTOR ANALYSIS OF SELF-REPORTED SYMPTOMS: DOES IT IDENTIFY A GULF WAR SYNDROME?

James D. Knoke, Ph.D.

Division of Epidemiology, Department of Family and Preventive Medicine,
School of Medicine, University of California, San Diego, CA

Tyler C. Smith, M.S., Gregory C. Gray, M.D., M.P.H.
Kevin S. Kaiser, M.P.H., and Anthony W. Hawksworth

DoD Center for Deployment Health Research, Naval Health Research Center, San Diego, CA

Introduction

Thousands of US veterans of the Persian Gulf War have reported varied symptoms and illnesses since the cessation of hostilities in March 1991. The diversity of symptoms reported has complicated the diagnosis of many of these veterans' conditions. The present study investigated the usefulness of factor analysis in characterizing a *Gulf War Syndrome*.

We performed a factor analysis using survey data from a group of Gulf War Veterans *(GWVs)*. We also performed a factor analysis using data from a control group of comparable nondeployed Gulf War era veterans (*NDVs*) and a third analysis using the combined GWV and NDV data. In this presentation, we will describe the five factors that emerged from these analyses. We will also estimate the number of individuals who are extreme for each factor and simultaneously for pairs of factors.

Methods

The study population consisted of US Naval Mobile Construction Battalion personnel (*Seabees*) who were on active duty in September 1990 and remained on active duty through 1994. This population included all 14 major Seabee commands that were based at either Port Hueneme, CA or Gulfport, MS. Since Seabees have frequent foreign deployments, extending up to six months a year, we made three visits to each of these sites (in late 1994 and early 1995) to recruit subjects.

Data were collected from a self-completed, computer-scanned survey questionnaire. This survey included, among other information, whether the respondent was deployed to the Gulf War and whether he or she experienced one or more of 98 symptoms. These symptoms included 57 questions detailed in the Hopkins Symptom Checklist (*HSC)* and 41 questions compiled at the Naval Health Research Center *(NHRC)*. These 41 questions included symptoms commonly reported by Gulf War veterans and several questions relating to depression. Also, one *validity* symptom, "earlobe pain," which is thought not to have a physiological basis, was included. Although the wording and the time period queried for symptoms were different, there was overlap between the two collections of questions. For example, the first symptom on the HSC is "headache," while the first symptom compiled by NHRC is "severe headache."

Details of the approach to factor analysis employed can be found in *American Journal of Epidemiology*, 152:379-388,2000. The symptoms comprising the factors that emerged from this analysis will be presented and discussed. The number of individuals who are extreme for each factor (greater than the 90th percentile of the NDV group) will be estimated, as will the percentage of individuals extreme for both of each combination of two factors.

Results

In September 1990, early in the Gulf War deployment period, there were approximately 15,400 active-duty Seabees. About 31% (4,700) of these Seabees were deployed. Approximately 55% of the active-duty Seabees (8,500) remained on active duty through 1994 and therefore were eligible for the present study. About 2,900 of these remaining Seabees were in residence at either Port Hueneme or Gulfport during one of the three visits made to each of these sites. Approximately 50% of the available Seabees agreed to participate, resulting in data on 528 GWVs and 968 NDVs. Since there were few women among the 528 GWVs, we restricted attention to men, resulting in 524 GWVs and 935 NDVs.

There were differences in the participation rates of GWVs and NDVs; 65% of available male GWVs participated, compared to 46% of available male NDVs. There were no significant demographic differences (age, race, marital status, and service-entry aptitude scores) between those who agreed to participate and those who did not. There may be other differences between participants and nonparticipants, however. For example, it is likely that participants reported more symptoms than nonparticipants would have reported.

GWVs studied were younger (by one year, on average), were more likely to be unmarried (27%, as compared to 22%), had completed less education (62% had only a high school education, as compared to 51%), and were more likely to be of enlisted rank (97%, as compared to 93%) than the NDVs studied. Race (76% white, 10% black, and 14% "other") was not significantly different between the GWV and NDV groups. Significantly more GWVs than NDVs reported most of the 98 symptoms. GWVs also scored significantly higher than NDVs on all five HSC categories.

We termed the five factors that emerged from the factor analyses as follows:

1. *Insecurity*, or minor depression. The symptoms primarily come from HSC categories 3, 4, 5, and 6.
2. *Somatization*. The symptoms primarily come from HSC category 1.
3. *Depression*. The symptoms primarily come from the NHRC questions relating to depression.
4. *Obsessive-compulsive*. The symptoms primarily come from HSC category 2.
5. *Malaise*. The symptoms primarily come from the NHRC questions relating to symptoms commonly reported by Gulf War veterans. They include a variety of miscellaneous symptoms and the *validity* symptom, earlobe pain.

There were about 70% more subjects extreme for factor 1 among the GWVs than among the NDVs. There were 120% to 150% more subjects extreme for factors 2, 3, and 4 among the GWVs than among the NDVs. The number of subjects extreme for factor 5 was approximately the same for both veteran groups, however.

Generally, there were similar proportions of subjects extreme on both factors, for each pair of factors, for both groups of veterans. Exceptions were for factor 3, for which the overlap with factors 1, 2, and 4 was greater in the GWV group, and for factor 5, for which the overlap with all other factors was less—for both veteran groups—than for other pairs of factors.

Discussion

The five factors found in our analyses were not unexpected, given that three were from the established, validated HSC and two were the categories of questions especially targeted by NHRC. The five factors that emerged from the GWV and NDV groups were similar, but the factors were generally stronger and involved more questions for the GWV group. The greater proportion of high positive factor scores among the GWVs for three of the factors was consistent with the factors being stronger for the GWV group, with the many veterans who have reported a variety of symptoms and illnesses since returning from the Persian Gulf War, and with the higher participation rate of GWVs. Elevated factor scores affected less than 30% of the GWVs, however.

Other investigators have performed factor analyses on different groups of GWVs and NDVs and have seen similar factors emerge from their GWV group as from their NDV group. Historically, the HSC investigators also found generally the same factors in a variety of populations, including hospitalized mental illness patients and healthy noninstitutionalized subjects, but with differences between populations in the magnitudes of the factor scores.

We believe that the symptoms and illnesses of GWVs closely reflect symptoms and illnesses reported by NDVs; GWVs simply participate at a higher rate and report more of the same symptoms and illnesses. Identifying a new syndrome such as the putative *Gulf War syndrome* is a difficult task and is unlikely to be accomplished by factor analysis, or any other statistical methodology, performed on a small, selected group of Gulf War veterans.

SINGLE AND MULTIPLE SYMPTOM-BASED CASE DEFINITIONS DESCRIBE PERSISTENT UNEXPLAINED ILLNESS IN GULF WAR VETERANS

A multidisciplinary group of clinical and non-clinical research scientists
represented by *Peter S. Spencer

Portland Veterans Affairs Medical Center and Oregon Health Sciences University's (OHSU)
*Center for Research on Occupational and Environmental Toxicology (CROET)
and School of Medicine, Departments of *Neurology and Medicine

Introduction

We have been engaged in studies to determine whether there is a detectable relationship between persistent unexplained illness among Gulf War veterans and their self-reported exposures to multiple stressors (chemical, biological, physical, psychological) in the 1990-91 theater of operations in S.W. Asia. These stressors were present in varying combinations over the course of operations between 8/1/90 and 7/31/91, a period of time characterized here as the Gulf War period.

Case-Control Clinical Study

Our first study analyzed risk factors and persistent unexplained illness in a population-based random sample of Gulf War veterans who underwent clinical evaluation. Multiple risk factors were compared in veterans who met criteria for persistent unexplained illness and in healthy control veterans. Persistent unexplained illness was diagnosed by the Portland study group when musculoskeletal pain, cognitive-psychological changes, *or* unexplained fatigue began during or after deployment to S.W. Asia, persisted for one month or longer, and occurred during the three-month period preceding recruitment into our case-control study. The U.S. Centers for Disease Control and Prevention (CDC) subsequently published a case definition that requires one or more chronic symptoms from *at least two* of three categories (fatigue, cognition, musculoskeletal [1]. We found similar associations between risk factors and persistent unexplained illness as defined by either the Portland or the CDC case criteria.

Our study population was all military personnel deployed to S.W. Asia during the Gulf War period who listed Oregon or Washington as their home-state-of-record at the time of deployment and who were believed to be residing (in 1995) in either of these two states. A random sample of 2343 veterans was selected, with over-sampling of women, reservists and veterans serving in discrete time periods specified below. These veterans were mailed a self-completion questionnaire that solicited information on (a) military service, duties, rank, dates and locations in S.W. Asia, (b) health history and symptoms experienced during and after the Gulf War (c) post-War lifestyle factors and psychosocial adjustment, and (d) exposures in the theater of operations. Only health-related information was used to recruit eligible subjects (N = 799) for the case-control clinical study. A committee that was blind to the exposure histories assigned cases (N=241) and healthy controls (N=113) on the basis of a review of the results of physical, mental status and neurological examinations, clinical laboratory testing, and specialist referrals. Of the 241 cases that met the Portland case definition, 115 met the CDC multi-symptom case criteria. The latter had significantly lower scores on the Armed Forces Qualifying Test and, compared to controls, U.S. Navy veterans were half as likely to be a case as those who served in the Army. There were no significant differences attributable to the primary job classification using either case definition.

Exposure Analysis

Preliminary analyses showed that the proportion of cases was distributed similarly among those deployed in S.W. Asia only within the pre-combat time period (8/1-12/31/90), only within the period surrounding Desert Storm (1/1-3/31/91), only within the period immediately following hostilities (4/1-7/31/91), or for various combinations of the three discrete deployment periods. This suggested that risk factors for persistent unexplained illness were present in S.W. Asia during Desert Shield, Desert Storm, *and* the post-War clean-up period. An examination of environmental factors potentially encountered by U.S. troops in the wartime theater showed that each period contained a different constellation of environmental stressors to which veterans were potentially exposed [3]. Noteworthy is our identification of cases of persistent unexplained illness in veterans who served only in the discrete deployments periods either before or after Desert Storm when there were reportedly no exposures to pyridostigmine bromide (PB), sarin, or botulinum toxoid vaccine [3].

Further analyses examined the relationship between self-reported exposures and persistent unexplained illness in the entire case-control study population For self-reported *single* exposures, the highest odds ratios (> 3.0) for both case definitions were found for the following:

- used insect spray on uniforms (permethrin),
- took more than 21 PB pills,
- contacted diesel/petroleum for six or more days,
- experienced irritated eyes from oil-well fire smoke for six or more days,
- worked in vehicle repair,
- exposed to depleted uranium,
- exposed to artillery smoke,
- exposed to welding fumes,
- sought medical attention during the Gulf War period.

Odds ratios were in general larger using the CDC case definition, but the confidence intervals were wider because of the smaller sample size. Additional odds ratios exceeding 3.0 were generated when the CDC case definition was employed:

- - was outside for 4 or more hours per day,
- - had a problem with flies in the living/eating area,
- - used diethyl-m-toluamide (DEET, insect repellant),
- - had inadequate MOPP gear during a chemical or SCUD alarm,
- - was bitten by snakes or scorpions.

Stress was measured using several measures from the survey questionnaire and scores on the Keane combat-exposure scale, a measure of exposure to potentially life-threatening combat experiences. Those with high Keane scores who used PB were four times more likely to be a Portland- and CDC-defined case than those who did not use PB. No such association was found for those with low Keane scores using either case definition. We were unable to demonstrate any interaction between stress and the *combination* of self-reported use of PB and insecticide. Exposure to PB was *not* significant in a multivariable model.

Forty-two exposure variables were subjected to an agglomerative hierarchical cluster analysis with complete linkage, which resulted in 9 clusters with at least two variables per cluster. Variables retained in the final model were found through backward elimination using the Akaike Information Criterion. Regardless of the case definition, the same demographic characteristics and three exposure clusters appeared in the final model. One cluster focused on seeking medical attention in the Gulf for flu-like symptoms, musculoskeletal problems or for a range of other conditions. With both case definitions, the odds of being a case increased in hand with the number of reasons for seeking medical attention. The second cluster included exposures associated with working outside, including time outside, heat-related symptoms, presence of flies in living/eating areas, and frequency of insect bites. The last cluster reflected combat activities in that it included self-reported exposure to depleted uranium, artillery smoke and fumes, working in areas where chemical warfare agents were found or stored, and the Keane combat-exposure scales. Clusters that did not enter the final model contained variables such as PB use, exposure to smoke from oil-well fires, use of DEET and permethrin, repair of generators and batteries, work with organic solvents and other chemicals, painting, welding, and consumption of alcoholic beverages.

Chemical Weapons

Our second study was designed to detect immediate and persistent health effects of low-dose exposure to chemical warfare agents, notably sarin. We conducted a telephone survey of 2918 Gulf War veterans currently (1998) residing in five U.S. states with over-sampling of veterans who had previously been notified by the U.S. Department of Defense as having been in an area of Coalition-occupied Iraq (Khamisiyah) where low-dose exposure to chemical warfare agents is likely to have occurred. Veterans in the Khamisiyah area during the time period in which artillery shells containing nerve agents were detonated (n= 653) were no more likely to report symptoms when compared to subjects not designated as being in the Khamisiyah area. However, 162 veterans in the Khamisiyah sample who reported they were involved in the detonation activity, or who were close enough to watch the detonations, were more likely to recall experiencing health effects consistent with those resulting from exposure to chemical warfare agents when compared to veterans in the Khamisiyah sample who did not observe the detonations. We performed

neurological examinations on a subsample of veterans in the Khamisiyah group (n= 42), veterans distant from Khamisiyah (n= 26) and non-deployed veterans (n= 28). Neurological and neurophysiological examinations designed to detect persistent effects of organophosphates revealed no group differences among these three groups. Furthermore, within the group receiving examinations, the seven veterans who witnessed Khamisiyah had similar neurological functioning to that of others who received clinical examinations. These findings are consistent with those reported in a study of the postwar hospitalization experience of Gulf War veterans exposed to the detonation at Khamisiyah [2].

Conclusion

Our findings add support to those of others that a case definition based exclusively on the presence of one or more related *symptoms* that arose during or after deployment to S.W. Asia during the Gulf War period accurately describes this illness. Our investigations have not revealed any evidence of an association between persistent unexplained illness in Gulf War veterans and exposures to chemicals that inhibit cholinesterase activity, including sarin, organophosphate pesticides, and PB. Neither these nor other single or combined chemical exposures in the theater of operations adequately explain persistent unexplained illness among Gulf War veterans

References

1. Fukuda K, Nisenbaum R, Stewart G, Thompson WW, Robin L, Washko RM, Noah DL, Barrett DH, Randall B, Herwaldt BL, Mawle AC, Reeves WC (1998) Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *JAMA* 280:981.

2. Gray GC, Smith TC, Knoke JD, Heller JM (1999) The postwar hospitalization experience of Gulf War Veterans possibly exposed to chemical munitions destruction at Khamisiyah, Iraq. *Am J Epidemiol* 150:532.

3. Spencer PS, McCauley LA, Joos SK, Lasarev MR, Schuell T, Bourdette D, Barkhuizen A, Johnston W, Storzbach D, Wynn M, Grewenow (1998) U.S. Gulf War Veterans: service periods in theater, differential exposures, and persistent unexplained illness. Portland Environmental Hazards Research Centre. *Toxicol Lett* 102-103:515.

This research was supported by the Department of Veterans Affairs through the former Portland Environmental Hazards Research Center, a joint initiative of the Portland VAMC and CROET at OHSU, and by a research grant to PSS from the U.S. Army Medical Research and Materiel Command (DAMD17-91-1-7353).

SUMMARY OF FIVE YEARS OF NEUROPSYCHOLOGICAL RESEARCH OF GULF WAR VETERANS AT THE PORTLAND ENVIRONMENTAL HAZARDS RESEARCH CENTER

Daniel M. Storzbach, Ph.D.

Oregon Health Sciences University, Portland VA Medical Center

Introduction

Significant numbers of US veterans who served in the 1991 Gulf War (GW) continue to report unexplained symptoms beginning during or after their deployment in southwest Asia. The US Departments of Veterans Affairs (DVA) and Defense (DOD) have conducted extensive examinations of self-selected GW veterans reporting health symptoms. Of the diverse symptoms reported by these veterans, problems with memory and attention are among the most common. Findings from previous investigations of war-related illness research have led some researchers to suggest that GW-associated symptoms result from psychological responses to war-related stress. Prominent alternatives to the stress-response hypothesis are various toxic exposure hypotheses.

In 1995, the Portland Environmental Hazards Research Center (PEHRC), a conjoint project of the Portland VA Medical Center and Oregon Health Sciences University, initiated a DVA-funded population-based case-control investigation of unexplained, nationally-reported GW symptoms seeking to identify factors that may contribute to their etiology. Both potential cases and asymptomatic GW veterans were identified by a questionnaire and telephone interview and then invited to participate in an all-day comprehensive medical and psychological evaluation. In addition to medical examinations and laboratory testing, veterans were administered a computerized batteries of neurobehavioral and psychological tests. Participants were classified as "cases" of Gulf War unexplained illness if they had unexplained cognitive, muscle-joint pain, or fatigue symptoms after the clinical evaluation. This multifaceted 5-year project resulted in several studies reporting neuropsychological findings.

PEHRC Studies Reporting Neuropsychological Findings

Ultimately 241 GW veterans with unexplained symptoms were classified as cases and 113 GW veterans without symptoms were classified as controls. Veterans were administered a computerized assessment battery consisting of 12 psychosocial and 6 neurobehavioral tests. Cases differed substantially and consistently from controls on diverse psychological tests in the direction of increased distress and psychiatric symptoms (Storzbach et al., 2000). Cases had small but statistically significant deficits relative to controls on some neurobehavioral tests of memory, attention, and response speed. A logistic regression model consisting of four psychological variables but no neurobehavioral variables classified cases and controls with 86% accuracy. Effect sizes for measures of psychological distress were much larger than those for neurobehavioral measures.

Because psychological distress effects were so much greater than neurobehavioral effects, follow-up studies examined the relationship of psychological factors to neurobehavioral performance. One study (Binder et al., 2000) compared GW veteran MMPI-2 profiles with epileptic seizure (ES) and nonepileptic seizure (NES) patient profiles, because NES and ES patients are well defined as somatoform and neurological groups, respectively. MMPI-2 profiles of 70 ES patients; 70 NES patients; 70 GW cases and 70 GW Controls were compared. GW Cases were mildly abnormal on MMPI-2 Scales Hs and D and significantly higher than controls on 8 of 10 MMPI-2 clinical scales, but they were significantly lower than NES patients on several scales, including those associated with somatization. Another study (Binder et al., 1999) analyzed the relationships between subjective cognitive complaints, affective distress, and cognitive performance in GW veterans who reported unexplained illness. In a sample of 126 veterans with cognitive complaints, correlations between a subjective cognitive complaints scale and depression and anxiety scales indicated a much larger relationship between subjective cognitive complaints and affective distress than between subjective cognitive complaints and any of the neurocognitive variables.

One consistent opinion to emerge from research on GW veterans is that unexplained GW symptoms may reflect a variety of illnesses or disorders rather than a single, unique syndrome. Assuming this is true, it would be reasonable to hypothesize that some but not all symptomatic veterans have neurocognitive impairment resulting from abnormal brain function. The existence of circumscribed subgroups of GW veterans with war-related changes in brain function would be especially likely for neurotoxic exposures that resulted from specific localized events. Among the first 101 GW veterans enrolled in the PEHRC case-control study investigators identified a subgroup of

symptomatic GW veterans with deficits on multiple neurobehavioral tests relative to other GW veterans (Anger, et al., 1999). These GW veterans with mild neurobehavioral impairment (MNI) performed significantly worse on measures of measures of memory, working memory, attention and response speed in comparison with both other symptomatic GW veterans and asymptomatic GW veterans, and constituted about 15% of symptomatic GW veterans in that sample. This initial study was later replicated and extended with the sample increased to 239 cases with unexplained symptoms and 112 controls (Storzbach et al., in press). Within the larger sample a MNI subgroup was again identified that demonstrated significantly reduced neurobehavioral performance relative to the rest of the sample, providing additional support for the hypothesis that there is a subgroup of symptomatic GW veterans who have objectively measurable neurocognitive abnormalities. However, the cause or causes of these abnormalities remain unknown.

Evidence of neurobehavioral differences was also demonstrated for the subgroup of cases in the PEHRC GW veteran study diagnosed with Chronic Fatigue Syndrome (CFS). This study (Binder et al., in press) tested the hypothesis that CFS is associated with cognitive deficits on computerized cognitive testing after controlling for the effects of premorbid cognitive differences using armed Forces Qualification Test (AFQT) data acquired around the date of induction into the military on 94 veterans of the Persian Gulf War, 32 with CFS and 62 healthy controls. Controls performed better than participants diagnosed with CFS on the AFQT. Cognitive deficits were associated with CFS on 3 of 8 variables associated with attention and mental processing speed after the effect of premorbid AFQT scores was removed with ANCOVA.

Summary and Conclusions

PEHRC studies reporting neuropsychological findings resulted in several conclusions. A nonclinical sample of GW veterans with unexplained symptoms demonstrated both increased psychological distress and diminished neurobehavioral performance. The psychological profile of GW veterans with unexplained symptoms differed from that of nonveteran patients diagnosed with conversion disorder. Subjective cognitive complaints of GW veterans were more strongly associated with psychological distress than with objective cognitive deficits. However, at least two subgroups of GW veterans were demonstrated to have objectively measurable neurocognitive abnormalities. One of these subgroups, identified by impaired test performance, demonstrated deficits on measures of measures of memory, working memory, attention and response speed and accounted for most of the neurocognitive differences between cases with unexplained symptoms and asymptomatic controls. The other subgroup, veterans diagnosed with CFS, demonstrated reduced attention and mental processing speed after statistically controlling for the effects of premorbid cognitive differences.

Overall, PEHRC neuropsychological findings are most consistent with the opinion to emerge from research on GW veterans that unexplained GW symptoms may reflect a variety of illnesses or disorders rather than a single, unique syndrome. Therefore better understanding of neuropsychological effects of GW unexplained illness is more likely to come from evaluation of specific subgroups. PEHRC results suggest that for a majority of symptomatic GW, psychological factors account for most of GW veteran's neuropsychological complaints. However, specific subgroups of symptomatic GW veterans have been demonstrated to have neuropsychological abnormalities independent of psychological distress and pre-GW level of functioning. The etiology could involve exposure to neurotoxic substances such as organophosphates in the Gulf, but there are other equally plausible explanations that have no relationship to service in the Gulf (e.g., health, lifestyle, occupation). More thorough neuroscientific investigation using such methods as brain imaging, quantitative EEG, and comprehensive neuropsychological evaluation could reveal other important, currently unrecognized factors associated with service in the Gulf.

The results summarized above are from the following studies:

Anger, W. K., Storzbach, D., Binder, L. M., Campbell, K., Rohlman, D., McCauley, L., Kovera, C., Davis, K., & members of the Portland Environmental Hazards Research Center (1999). Neurobehavioral deficits in Persian Gulf War veterans: Evidence from a population-based study. Journal of the International Neuropsychological Society, 5, 203-212.

Binder, L. M., Storzbach, D., Campbell, K., Anger, W. K., Rohlman, D., McCauley, L., Davis, K., Kovera, C., & members of the Portland Environmental Hazards Research Center (1999). Subjective cognitive complaints, affective distress, and objective cognitive performance in Persian Gulf War veterans. Archives of Clinical Neuropsychology, 6, 531-536.

Binder, L. M., Storzbach, D., Campbell, K., Rohlman, D., Anger, W. K., & members of the Portland Environmental Hazards Research Center (in press). Neurobehavioral deficits in in Gulf War veterans with chronic fatigue. Journal of the International Neuropsychological Society.

Binder, L. M., Storzbach, D., Campbell, K., Rohlman, D., Anger, W. K., Salinsky, M. C., Campbell, B. M., & Mueller, R. (2000). Comparison of MMPI-2 profiles of Gulf War veterans with epileptic and nonepileptic seizure patients. Assessment, 7, 73-78.

Storzbach, D., Campbell, K., Anger, W. K., Binder, L. M., Rohlman, D., McCauley, L. & members of the Portland Environmental Hazards Research Center (2000). Psychological differences between veterans with and without Gulf War unexplained symptoms. Psychosomatic Medicine, 62, 726-735.

Storzbach, D., Rohlman, D., Anger, W. K., Binder, L. M., Campbell, K., & members of the Portland Environmental Hazards Research Center (in press). Neurobehavioral deficits in Persian Gulf veterans: Further evidence from a population-based study. Environmental Research.

NEUROPSYCHOLOGICAL FUNCTIONING IN PGW VETERANS: STUDIES FROM BEHC

Roberta F. White, Ph.D.

Boston Environmental Hazards Center, Boston VA Healthcare System,
Boston University Schools of Medicine, Public Health and
Arts and Sciences, Southern Denmark University School of Medicine

rwhite@bu.edu

Introduction

Many of the complaints voiced by Persian Gulf War veterans after their return from the conflict were suggestive of central nervous system (CNS) dysfunction. These included memory loss, problems with concentration, fatigue and headaches. Possible exposures in the Gulf that might be associated with CNS dysfunction include chemicals with neurotoxic properties such as pesticides and chemical warfare agents and the stressors experienced as part of deployment to and action in the Gulf. Neuropsychological test methodology is one means of objectively quantifying subtle brain dysfunction resulting from structural and/or neurotransmitter pathology. At BEHC we launched a series of studies in which we applied this methodology to a number of groups of PGW veterans and controls, at the same time examining chemical exposures, veterans' locations in the Gulf war theater, stress symptomatology, psychiatric status, and symptoms of ill-defined multi-system disorders.

Objectives

Determine whether there are neuropsychological deficits associated with PGW deployment in the general PGW veteran population that are not seen in appropriate controls. Explore differences in symptom complaints and neuropsychological test findings in treatment-seeking deployed PGW veterans when these veterans are compared to non-treatment seekers and to non-deployed PGW-era veterans. Examine the relationship between exposures to chemicals in the Gulf and neuropsychological function. Evaluate differences in neuropsychological functioning among PGW veterans who spent time in different locations in the Gulf theater. Determine rates and effects of diagnosable psychiatric disorders and of syndromes such as post-traumatic stress disorder (PTSD), chronic fatigue syndrome (CFS) and multiple chemical sensitivity (MCS) on cognitive test results. Evaluate the effects of intensity of stress (less than that required for a diagnosis of PTSD) on neuropsychological test findings. Explore the possibility of malingering or embellishment as an explanation of neuropsychological test scores. Examine non-American PGW veterans to determine if neuropsychological deficits are observed relative to appropriate controls. Use other methods of examining brain function to validate the findings based on psychometric tests.

Methods

PGW deployed veterans studied included two large cohorts that were examined shortly after their return from the Gulf (Ft. Devens and New Orleans samples); these groups were divided into high and low health-symptom reporters, which were compared to each other and to a National Guard unit from Maine. A second type of sample was recruited from PGW-era veterans who sought treatment for various symptoms and conditions at the Boston VA Healthcare system; this group included PGW-deployed veterans and era veterans who were not deployed to the Gulf. Also studied was a sample of Danish military personnel who were sent to the Gulf after the war and a Danish control group. In all of these studies, subjects underwent a battery of neuropsychological tests, answered questions about their physical symptoms, were interviewed about their chemical exposures and sites where they spent time in the Gulf, were administered the Clinician Administered PTSD Scale (CAPS) and the Mississippi PTSD scale, and completed a psychiatric diagnostic interview. The outcome measures were scores on neuropsychological tests, which were evaluated in terms of self-reported chemical exposures, severity of stress symptomatology, self-reported neuropsychological symptoms, performance on a test of motivation or malingering, and degree of health symptomatology (high vs. low). Relevant moderator variables were included in the analyses, including gender, age, branch of service, education, scores on tests that are considered to be accurate indicators of premorbid intelligence, history of learning problems in school, psychiatric diagnosis, PTSD diagnosis, and application for disability.

Findings to Date

Among the general population of deployed PGW veterans, those with self-reported exposure to pesticides reported more mood complaints than those not reporting such exposure. Veterans with self-reported exposure to chemical/biological warfare agents performed more poorly on several neuropsychological measures than those without such exposures. Self-reported exposure to pyridostigmine bromide (PB) was not associated with any decrement in neuropsychological test performance. None of these findings is explainable on the basis of severity of stress symptoms or malingering, although these factors did affect scores on some neuropsychological tasks. Among treatment seeking PGW-era veterans, deployed veterans performed significantly more poorly than non-deployed veterans on a number of neuropsychological tests. In this group, PB exposure was associated with decrements on some tests. Rates of diagnosis of MCS, CFS and PTSD were too low among the veterans to examine the effects of these disorders on neuropsychological test results.

Future Directions

In a new study we are re-examining the PGW-era veteran treatment-seekers to determine if complaints of progressive cognitive change in the deployed group are evident on objective testing. We are also attempting to apply geographical information system techniques to determine if location while in the Gulf is associated with neuropsychological deficit. A study is underway in which we are exploring the neuropsychological test findings on PGW veterans using functional magnetic resonance imaging techniques.

ASSESSMENT OF COGNITIVE DYSFUNCTION IN GULF WAR VETERANS: THE IOWA GULF WAR CASE-VALIDATION STUDY

J. Barrash[1], R.F. Woolson[2], M.D. Voelker[2,3], J.E. Holman[3], A. Schumacher[1], M.M. Adams[3] & B.N. Doebbeling[3,4,5]

Departments of Neurology[1], Biostatstics[2], Internal Medicine[3] and Epidemiology[4], Colleges of Medicine and Public Health, University of Iowa, Iowa City, IA, and Veterans' Affairs Medical Center[5], Iowa City, IA

joseph-barrash@uiowa.edu

Introduction

Problems with concentration, memory and mental functioning generally have been among the most frequent complaints of Gulf War–deployed veterans (GWD). Cognitive deficits are not only problems in their own right, but are also of concern as possible manifestations of underlying cerebral dysfunction. Assessment of cognitive complaints and their etiologies among GWD present methodologic challenges which have limited our ability to draw clear conclusions from the extant literature. A few particularly important concerns include: (a) Sampling issues: Many investigations have studied a non-random set of GWD, e.g., those who have presented with cognitive complaints, or who come from a selected unit. The findings from such selected samples may not be representative of GWD in general, and may be misleading. (b) Assessment issues: Some studies rely on GWD's self-reported cognitive functioning, which are of uncertain accuracy. Formal neuropsychological assessment of cognitive functioning, blinded to study group, is more objective, however the validity of such assessment depends on the motivation and effort of examinees. (c) Analytic issues: Studies of cognitive problems among GWD have typically relied on group analyses, i.e., determining whether the mean performance of a group of GWD is significantly lower than the mean performance of an appropriate comparison group. Group means may fail to reveal impairments which exist in a subset of subjects, or conversely, may exaggerate the extent of impairment in the group. Furthermore, if impairments exist in some GWD and not in others, group means do not reveal the prevalence of impairment. The present study was designed with these methodologic concerns in mind. In this abstract we describe our methodologic and analytic approach to investigating the validity and prevalence of complaints of cognitive dysfunction among GWD and among Gulf War-era veterans not deployed to the Gulf (GWE).

Initial Sampling

In the initial phase of the Iowa Gulf War Study, a structured telephone survey was conducted 5 years post-conflict to determine the prevalence of complaints in several aspects of health and quality of life (The Iowa Persian Gulf Study Group, *JAMA*, 1997). An important feature of the Iowa Gulf War study was its rigorous, unbiased sampling from a sizeable population: the 29,000 veterans eligible for Gulf War deployment listing an Iowa address at the time of enlistment. From that population, 4,886 study subjects (Ss) were randomly selected from 1 of 4 study domains (GWD regular military, GWD national guard/reserve, GWE regular military, GWE national guard/reserve), stratifying for age, sex, race, rank and branch of service. 3,695 Ss (76% of the sample, 91% of all located Ss) completed the telephone interview, in which information regarding symptomatology and functioning was obtained with validated measures.

Identification of Self-Reported Cognitive Dysfunction (CD-SR): Case Definition

Prior to the phone interviews, an operational definition of CD-SR was specified which incorporated the presence and severity of self-reported symptoms in key domains of cognitive functioning. The definition required: (a) problems with severe memory impairment; (b) being at least moderately bothered by confusion or disorientation; (c) being moderately bothered by at least two of the following: problems thinking clearly, difficulty concentrating, difficulty comprehending, difficulty with reading comprehension, slips of the tongue, forgetfulness, memory problems, or periods of confusion or disorientation; or (d) being bothered quite a bit by any one of the above. The construct validity of this case definition was supported by relationships between case status and outcomes, including health care utilization, disability, and health-related quality of life, assessed with the Short Form-36 (Barrash et al., 2001). By that definition, 19% of the GWD had CD-SR, a significantly higher rate than GWE (8%). CD-SR was the most frequently reported health-related condition among GWD, along with fibromyalgia (19%).

Sampling for Case Validation

To investigate the validity of GWD self-reported health conditions, the Iowa Gulf War Study Group has undertaken a nested case-validation study of the 3 most prevalent outcomes reported by GWD on phone interview: fibromyalgia, CD-SR and depression. At present, 157 GWD and 141 GWE -- selected by stratified random sampling of Ss completing the phone survey – have participated in extensive in-person assessment including formal neuropsychological testing. The estimated overall participation rate at this point is 63%.

Neuropsychological Assessment

Neuropsychological assessment is the first of several evaluations study participants undergo. After a brief interview regarding background characteristics and neurologic history, Ss are administered the following battery of neuropsychological tests: North American Reading Test-Revised (NART-R: estimate of premorbid intellect), Similarities (verbal reasoning), Block Design (nonverbal reasoning, visuoconstruction), Digit Span (concentration, immediate memory), Digit Symbol (nonverbal learning, visuomotor speed), Controlled Oral Word Association Test (COWA: expressive language, sustained attention), Rey Auditory Verbal Learning Test (AVLT, verbal learning and memory), Benton Visual Retention Test (BVRT: immediate visual memory, concentration), Recognition Memory Test – Words & Faces (RMT: verbal and visual memory, respectively), Stroop Test (executive functioning), Trail Making Test (visual scanning, visuomotor speed, mental tracking, executive functioning), Starry Night Test (sustained visual attention, simple reaction time), Grooved Pegboard Test (manual dexterity), and Minnesota Multiphasic Personality Inventory-2 (MMPI-2: psychological status, test-taking attitude). The assessment incorporates measures to assess motivation and effort. The battery takes approximately 2.75 hours to complete. Performances are scored blindly.

Assessment of Co-Morbid Conditions

In addition to neuropsychological assessment, the day-long assessment includes standardized assessment by an MD of history and physical, family history, review of systems, and ratings of disability; MD evaluation of fibromyalgia-related symptomatology; Ss' self-report of health and well-being, occupational exposure, social support, and post-traumatic stress symptomatology; and evaluation of psychological functioning and psychiatric status by standardized psychiatric interview (SCID-IV, GAS) and several self-report measures. Blood samples are being collected and stored at –70°C; a subset of symptomatic GW veterans undergo lab tests.

Analysis of Neuropsychological Data

A major feature of the Iowa Study is analysis of the individual. That is, we determine the presence and severity of cognitive dysfunction for each individual subject. This individual analysis allows for (a) determination of the rate at which GWD and GWE Ss' CD-SR (by phone survey) are validated, and (b) comparison of the prevalence of CD-V among GWD vs GWE. Determination of impairment will be performed in a two-step process: First, performances on individual tests will be characterized as "normal," "mildly impaired," or "moderately to severely impaired." Secondly, the presence and degree of impairment across tests will be considered in order to characterize overall cognitive functioning as "normal," "mildly impaired," or "moderately to severely impaired."

First, impairment on individual tests is operationalized as a significant decline in a specific ability in comparison to an individual's expected level (i.e., estimated premorbid level) rather than in comparison to a broad normative group, an approach espoused by Lezak (1995). A S's expected performance will be based on their age, gender, education, and premorbid intellect (as estimated by the NART-R). Equations to arrive at a S's expected performance on any specific measure will be derived by regression analyses of the relationships of test scores to age, gender, education, and NART-R score of approximately 100 normal controls (i.e., GWE denying cognitive difficulties). A score which falls one standard deviation (SD) below a S's expected score on a given measure (i.e., below the 16th percentile, given a normal distribution) will be characterized as "mild impairment", scores 1.5 SDs below the expected score (< 7th %ile) will be characterized as "moderate impairment", and scores 2 SDs below the expected score (< 3rd %ile) will be characterized as "severe impairment."

Regarding the characterization of overall cognitive functioning, cases of self-reported cognitive dysfunction (CD-SR) will be considered validated (CD-V) if: (a) their neuropsychological performances include mild impairment on at least two tests, or moderate to severe impairment on at least one test, and (b) the neuropsychological exam does not provide evidence of inadequate effort or intent to exaggerate problems.

Evidence for (b) will come from validated measures for detecting inadequate effort which are built into the exam; from a rating of effort based on specified behavioral guidelines, completed by the technician (blinded to exposure status); and from well-established MMPI-2 "validity scales."

Analysis of Contributing Factors to Cognitive Dysfunction

The protocols of all Ss meeting the above criteria for CD-V will be examined for the presence of factors that might contribute to CD-V. These include: (a) exposure to neurotoxins during deployment to the Gulf theater, (b) history of other neurologic insults including traumatic brain injury and substantial alcohol/drug abuse, (c) co-morbid medical conditions that have been associated with cognitive dysfunction (e.g., poorly-controlled diabetes mellitus, chronic fatigue syndrome), (d) medications with cognitive dulling side effects, and (e) psychiatric conditions. Analysis will consist of determining the rates of specific contributing factors among Ss with CD-V.

Neurophysiological aAssessment

A subset of Ss will undergo neurophysiological assessment to validate CD-V primarily attributable to neurological/medical factors (see 9.2 below). Approximately 100 Ss with CD-SR and controls are being evaluated using the blink reflex test. Brain stem auditory and somatosensory evoked potential tests will be conducted on a random sample of 60 CD-V cases and normal controls (i.e., normal cognitive functioning by self-report and by neuropsychological assessment).

Hypotheses

(1a) CD-SR among GWD will be validated in most cases. (*The rate of CD-V, in conjunction with findings from the original telephone survey, will provide an estimate of the true rate of cognitive dysfunction among GWD.*) (1b) However, it is expected that there is a non-negligible percentage of CD-SR cases whose complaints will not be validated. It is hypothesized that the rate at which CD-SR fails to be validated by neuropsychological evaluation does not differ between GWD and GWE, a finding which would suggest negligible bias in the reported rate of CD-SR *due to GWD status*. (2) There are clinically distinct subsets among GWD with CD-SR: (a) CD-V primarily attributable to neurological/medical factors, (b) CD-V primarily attributable to psychiatric factors, and (c) CD-SR primarily attributable to inadequate effort/motivation. It is hypothesized that these subsets differ significantly in their neuropsychological profile, rates of neurophysiological abnormalities, psychological profile, psychosocial characteristics, and medical resource utilization. (3) The rates at which CD-SR is associated with primarily medical/neurological, psychiatric or motivational factors do not differ significantly between GWD and GWE.

This work was partially supported by CDC Cooperative Agreement, U50/CCU711513, and DOD Grant #DAMD17-97-1-7355. Dr. Voelker was also supported by NIH training grant #5 T32 MH15158-23.

A CONTROLLED STUDY OF NEUROPSYCHOLOGICAL FUNCTIONING AND MOOD DISORDER IN U.K. VETERANS OF THE GULF WAR

Anthony S. David, Lydia Farrin, Lisa Hull, Catherine Unwin, Til Wykes, Simon Wessely

Gulf War Illnesses Research Unit, GKT School of Medicine, King's College, London

a.david@iop.kcl.ac.uk

Complaints of poor memory and concentration and mood changes are common in Persian Gulf War (GW) veterans. In a comprehensive survey of UK military personnel who served in the GW, irritability and anger was reported by 55%, while forgetfulness and loss of concentration was reported by 50% and 45%, respectively (Unwin et al, 1999). Clinical evaluations in the UK, USA and Denmark confirm these reports. To date only a small number of studies have been published specifically investigating the neuropsychological performance of veterans and no consistent findings have emerged. Hence while there is a well replicated high prevalence of cognitive and emotional disturbances in surveys of GW veterans several years after the conflict, there is no clear evidence for cognitive deficits on detailed testing. The possible reasons for objective cognitive impairment in this group (of whatever degree) include neurotoxic exposures - as advanced by Haley and others, and information processing deficits secondary to depression or anxiety. One explanation for the subjective-objective discrepancy is cognitive bias leading to negative performance evaluation by those veterans with low mood.

We tested 341 UK returnees from the Gulf and Bosnia, and non-deployed military controls drawn from a large randomized survey; most were selected with impaired physical functioning as defined by a cut-off on the Medical Outcomes Scale, SF-36 (below the 10th centile of the Era groups scores) along with well Gulf veterans. Subjects were invited to attend the research unit for a detailed physical and psychological evaluation. A battery of tests and self-report questionnaires was administered. This included measures of: general intellectual functioning, Wechsler Adult Intelligence Scales–revised (WAIS R), the Wechsler Memory Scale (WMS), and the National Adult Reading Test (NART) as an estimate of premorbid IQ; attention and vigilance: the Paced Auditory Serial Addition Task (PASAT), and Sustained Attention to Response Task (SART); executive function: the Stroop and Trails tests; and motor skill: the Purdue Pegboard. In addition self report scales such as the Cognitive Failures Questionnaire (CFQ), Beck Depression Inventory (BDI), State-Trait Anger Expression Inventory (STAXI) and Mississippi Combat Related PTSD Scale were completed.

In total there were 209 GW veterans, 78 'Era' and 54 former Bosnia peace-keepers. Ages ranged between 22 and 62 years, with the Gulf group being the eldest. Out of the 341, 25 were female; 284 were Army, 31 Royal Air Force and 26 Navy. 252 were educated to high school standard, and 88 had the equivalent of a college diploma or above. 41.3% of subjects were still serving.

According to health status at the time of testing, there were 76 Gulf ill, 36 Bosnia ill and 36 Era ill; and 131 Gulf well, 18 Bosnia well and 39 Era well. A 3 X 2 ANCOVA was used to compare the six groups on the test variables with deployment (Gulf, Era, Bosnia) and current health status (well, ill) as the factors. The analysis covaried for (i) age, education and NART-estimated IQ, and (ii) for these potential confounders plus BDI depression score. Least Significant Difference post hoc procedure (alpha set at 0.05 = ✓; X = non-significant) was used to identify significant differences between groups (see Table below).

Group comparisons revealed an association between impaired physical functioning and symptoms of depression, post-traumatic stress disorder (PTSD), increased anger and subjective cognitive failures. Poorer performance on some general cognitive measures (such as performance IQ), and those of sequencing and attention was seen in association with being 'ill' but virtually all differences disappeared after adjusting for depressed mood. Deployment (to the Gulf *and* Bosnia) was also associated with symptoms of PTSD and *subjective* cognitive failures independently of health status as well as minor general cognitive (WAIS verbal IQ) and constructional impairment (the Purdue Assembly measure). Higher IQ and CFQ scores were associated with deployment to the Gulf and Bosnia while Purdue scores remained significantly poorer in the Gulf group alone even after adjusting for depressed

mood (✓✓). The absolute levels of performance were within the normal or average range, eg., mean VIQ (S.D.) Gulf ill = 94.6 (10.3); PIQ Gulf ill = 102.1 (13.7). There were no significant interactions between deployment and health status.

Test	*Main Effects*	
	SF-36	*Deployment*
BDI	✓	X
Mississippi	✓	✓
STAXI –Trait anger	✓	X
CFQ	✓	✓✓
WAIS-VIQ	X	✓✓
WAIS-PIQ	✓	✓
Trails	✓	X
Stroop	X	X
PASAT	X	X
Attention/Vigilance	X	X
Learning/Memory	X	X
Purdue All	X	~
Purdue Assembly	X	✓✓

Finally, an alternative means of dealing with depressed mood as a potential confound was attempted. We stratified the original Gulf 'ill' participants according to BDI score, above and below the suggested cut-off of 10 for 'mild .; The only specific neuropsychological measure which differentiated 'non-depressed' participants from the three deployment cohorts, after adjustments, was the Purdue Pegboard, (right hand scores only; not assembly) although levels of anger, PTSD and even BDI scores were higher in the Gulf group. Full scale IQ also differed (p=0.04) with the mean scores for Gulf (101.0) being significantly lower (p=0.02) than Bosnia (105.6) and nearly significantly lower (p=.09) than Era (103.7).

In conclusion, the results from our studies and most published work so far reaches a consensus that there is no objective neurocognitive deficit syndrome attributable to service in the Gulf wWar. Nevertheless, we have demonstrated yet again that emotional and psychological disorder is common in GW veterans and, in a minority, likely to be clinically significant. Disturbances of mood probably lead to subjective underestimation of ability. Task performance deficits can themselves be explained to a large extent by depressed mood. Those weak effects which were detected were patchy in terms of the cognitive systems implicated. Furthermore they were just as likely to be attributable to any active deployment and hence not likely to be related to specific Gulf-related exposures – with the exception of the Purdue Assembly measure. Test performance in unwell veterans was impaired relative to well controls but generally within the normal range. However, reduced constructional ability on the Purdue Assembly sub-test cannot be explained in this way and could be an effect of Gulf-specific exposures. Such a specific deficit – other Purdue variables tending to be normal - defies an obvious pathophysiological explanation. Further research of neuromotor coordination in Gulf War veterans would be valuable.

This research was supported by U.S. Department of Defense.

US DEMOLITION OPERATIONS AT KHAMISIYAH

The Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses has published the story of US Demolition Operations at Khamisiyah. The story has three parts:

- United States military operations including demolition of Iraq's munitions at Khamisiyah;
- United Nations Special Commission on Iraq (UNSCOM) inspections of Khamisiyah, which brought to light the presence of chemical weapons at various locations on and around the site; and
- The US government response to mounting indications that US soldiers may have destroyed chemical munitions at Khamisiyah—the details of what the Department of Defense knew, when it knew them, and the actions it has taken.

A. United States Military Operations at Khamisiyah

Immediately following the end of Operation Desert Storm, US Army units occupied an area in southeastern Iraq that encompassed Khamisiyah (also known then as the Tall al Lahm Ammunition Storage Area). Soldiers of the Army's XVIII Airborne Corps conducted two large-scale demolition operations to destroy the munitions and facilities around Khamisiyah:

- March 4, 1991. Soldiers destroyed 37 large ammunition bunkers. Later, Iraq declared that one of these, Bunker 73, had contained 2,160 chemical warfare agent-filled rockets.
- March 10, 1991. Soldiers destroyed approximately 40 additional ammunition bunkers and 45 warehouses. In an open-air location outside the Khamisiyah Ammunition Supply Point (ASP) now known as "the Pit," soldiers also destroyed approximately 1,250 rockets, many of which UNSCOM later found had contained chemical warfare agent.

Soldiers also conducted numerous demolitions to destroy smaller caches of munitions and to test techniques for destroying bunkers. The 2nd Armored Cavalry Regiment continued demolition operations in the Khamisiyah area through the middle of April 1991. The soldiers who conducted reconnaissance and completed the inventories before these demolitions were confident that they had destroyed only conventional munitions. Throughout the US occupation of Khamisiyah, including the demolition period, no reports were made of chemical warfare agent detections. Nor were there reports of anyone—soldier or civilian—experiencing symptoms consistent with chemical warfare agent exposure.

B. United Nations Special Commission on Iraq Inspections at Khamisiyah

In October 1991, March 1992, May 1996, and in 1998, UNSCOM inspected Khamisiyah. In October 1991, Iraqi officials led UNSCOM inspectors to three sites that had contained chemical weapons (Figure 1):

- Bunker 73, inside the Khamisiyah ASP;
- The area referred to as the Pit, outside the southeast corner of the Khamisiyah ASP; and
- An above-ground storage area, approximately 3 kilometers from the Khamisiyah ASP.

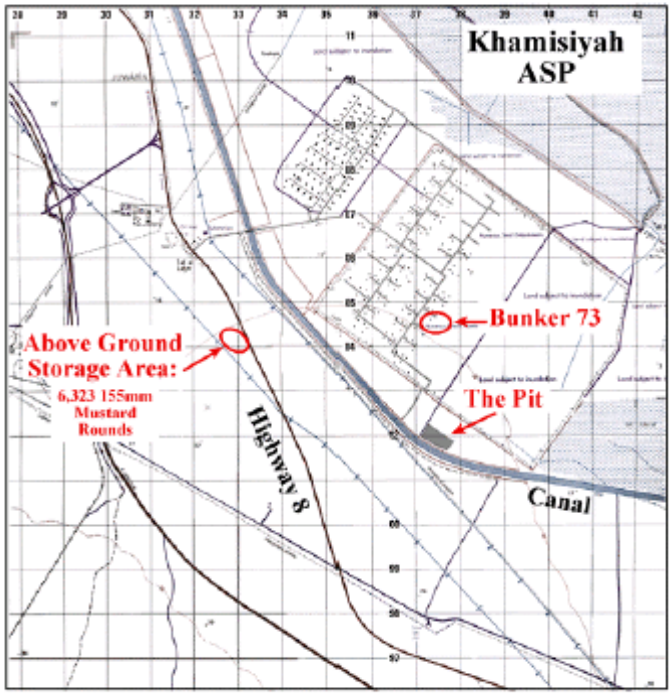

Figure 1. Site locations shown to UNSCOM

Bunker 73. During the 1991 inspection, Iraq claimed that chemical munitions found in the Pit had been salvaged from Bunker 73 and that Coalition forces had destroyed the bunker. UNSCOM could not determine if Bunker 73 contained chemical warfare agents at this time because damaged munitions made it too dangerous to get close enough to sample or take Chemical Agent Monitor readings. However, on a return visit to the site in May 1996, UNSCOM conclusively determined that debris (e.g., burster tubes, fill plugs, and plastic inserts) in the rubble of Bunker 73 was characteristic of chemical munitions.

The Pit. In October 1991, UNSCOM inspectors found several hundred 122mm rockets that appeared to have been bulldozed and placed into piles in an excavated area southeast of the main ASP. This area became known as the Pit. The UNSCOM investigation showed that the intact rockets contained the chemical warfare agents sarin and cyclosarin. During a subsequent visit in March 1992, UNSCOM ordered Iraq to destroy about 500 leaking rockets near the Pit and ship the remaining rockets to Al Muthanna, Iraq, for destruction. UNSCOM supervised Iraqi destruction of a total of approximately 782 rockets at both the Pit and Al Muthanna.

Above-ground storage area. Iraq also showed the UNSCOM team an above-ground storage site about 3 kilometers west of the Khamisiyah ASP that contained 6,323 intact 155mm artillery shells, one of which was leaking mustard agent. No evidence exists that any Coalition forces had been to this site. Again, UNSCOM ordered Iraq to ship these rounds to the destruction facility at Al Muthanna.

In November 1991, US intelligence and DoD became aware of the UNSCOM findings, but at the time, did not identify which, if any, US troops participated in the Khamisiyah demolition activities. The lack of US reports of chemical weapons, combined with Iraq's less than full compliance with UNSCOM, led to doubts about Iraq's claims that chemical weapons had been at the site when the demolition occurred.

C. The United States Government Response Regarding Illnesses of Gulf War Veterans

The US government did not immediately make the connection between the chemical munitions found by UNSCOM at Khamisiyah and US demolition operations there. However, increased complaints from Gulf War veterans prompted government investigations and in March 1995 the Central Intelligence Agency began a reexamination of relevant intelligence. In 1994 a request from Congressman Browder to the United Nations (UN) for any reports about chemical weapons found in Iraq after the Gulf War kindled DoD interest in Khamisiyah. The United Nations responded in April 1994 with a letter that listed Khamisiyah along with other chemical weapons sites. In June 1995 the DoD formed the Persian Gulf Investigation Team (PGIT) that by October had identified some of the US forces that had occupied the area around Khamisiyah during the Gulf War, including the 37th Engineer Battalion. In June 1996 the DoD confirmed publicly that "US soldiers from the 37th Engineer Battalion destroyed ammunition bunkers [at Khamisiyah] in early March 1991 ... It now appears that one of these destroyed bunkers contained chemical

weapons." The Secretary of Defense established the Office of the Special Assistant for Gulf War Illnesses in November 1996 to focus ongoing DoD investigations and expand the investigation into Gulf War veterans' complaints of undiagnosed illnesses.

The early work of the Office of the Special Assistant placed an emphasis on researching US military operations at Khamisiyah. On February 21, 1997, we published the first Khamisiyah case narrative. The narrative provided important insights into what actually took place and which US military units were involved. We intensified our efforts to identify and contact the thousands of soldiers potentially involved, and began detailed computer modeling of events in the spring and summer of 1997 to determine the size and path of the potential hazard area created by demolition activities in the Pit. The modeling resulted in DoD sending notification letters to approximately 99,000 veterans. Letters were mailed to those veterans thought to have been possibly exposed and also to an additional 10,000 veterans who previously responded to a questionnaire about Khamisiyah, but whose unit was not in the 1977 potential hazard area.

Modeling refinements continued through 1998 and 1999. Some of the more significant modeling refinements included revision of meteorological models, an updated Central Intelligence Agency estimate of how much chemical warfare agent was released, modeling the effects of deposition and decay, consideration of toxicity of both sarin and cyclosarin in the models, and vastly improved troop unit locations. The modeling team completed remodeling the Khamisiyah Pit demolition in January 2000 resulting in a redefined potential hazard area. Unit location data improvements and a scientific and technical peer review of the work were completed in September 2000. DoD identified 100,923 veterans in the 2000 potential hazard area who possibly were exposed to low levels of nerve agent. As a result of modeling improvements and greater refinement of troop unit locations some veteran's units which were in the 1977 potential hazard area are not in the 2000 potential hazard area. Likewise, some units that were not in the 1997 potential hazard area fell in the 2000 hazard area. There were also units identified in 1997 that remained in the 2000 hazard area. All affected veterans were mailed letters explaining the modeling results. Our fundamental modeling methodology has not changed since 1997. In 2000, like 1997, we used the outer boundaries of the union of the results from different models to define the potential hazard area. This approach gave us greater assurance of identifying US units in the potential hazard area. The veterans' notification process is ongoing.

The narrative includes the following conclusions:

- Chemical munitions were definitely present at three locations at Khamisiyah.
- US soldiers definitely destroyed many—but not all—of the chemical rockets at Khamisiyah.
- Some US ground forces were likely exposed to very low levels of nerve agent from the demolition of rockets in the Pit on March 10, 1991.
- It is unlikely US ground forces were exposed to chemical warfare agent from the Bunker 73 demolition on March 4, 1991.

REPORT OF THE INSTITUTE OF MEDICINE COMMITTEE ON HEALTH EFFECTS ASSOCIATED WITH EXPOSURES EXPERIENCED DURING THE PERSIAN GULF WAR

Harold C. Sox

Department of Medicine, Dartmouth-Hitchcock Medical Center

harold.c.sox@dartmouth.edu

In response to a request from the Department of Veterans Affairs (VA), the Institute of Medicine (IOM) conducted a study to evaluate the published scientific literature concerning the association between the agents to which the Gulf War veterans may have been exposed and adverse health effects. The committee selected the compounds of most concern to the veterans: depleted uranium, chemical warfare agents (sarin and cyclosarin), pyridostigmine bromide, and vaccines (anthrax and botulinum toxoid). Additional IOM studies will examine other agents to which the veterans may have been exposed.

The committee reviewed all relevant studies published in peer-reviewed journals. Because only a small number of studies directly involved Gulf War veterans, the committee extended its review to include research involving any human population that had contact with these agents at any dose. It carefully assessed the quality, limitations, and applicability of each study and used five categories to describe the strength of all the evidence.

The committee's charge was to conduct a review of the scientific literature on the possible health effects of agents to which Gulf War veterans may have been exposed. The breadth of this review included all relevant toxicological, animal, and human studies. Because only a few studies describe the veterans' exposures, the committee reviewed studies of any human populations—including veterans—that had been exposed to the agent of concern at any dose. These studies come primarily from occupational, clinical, and healthy volunteer settings. The committee reviewed these studies in order to draw conclusions about associations between the agents of interest and adverse health effects in all populations.

When it comes to the *long-term* health effects of these substances, the bottom line is we simply don't know enough to say whether there is a connection between exposure to these agents or combinations of agents and specific health outcomes that remain long after the exposure. At most, we found some very limited evidence that might suggest a possible connection with the nerve agent sarin. These effects, if they truly exist, occur in individuals whose dose was large enough to cause acute symptoms immediately after the exposure. It will take further research to explore this relationship.

FORCE HEALTH PROTECTION: NEW STRATEGY TO PROTECT DEPLOYED FORCES

Robert G. Claypool, M.D.

Executive Director, Military and Veterans Health Coordinating Board

Robert.claypool@hq.med.va.gov

The ultimate weapon in today's military is not a particular piece of hardware but rather is the service member himself or herself. Modern warfare platforms are so complicated that a considerable investment must be made in training the men and women who man them. Yesterday, if a soldier, sailor, airman, or marine was taken out of commission by illness or injury, it was not usually a difficult task to swiftly plug in a replacement. Today, the loss of a highly trained "technical warrior" runs the risk of jeopardizing the military operation because a replacement isn't necessarily an assured thing. In addition, accrual training costs dictate the necessity of viewing our service personnel as 'expensive weapons systems' whose life cycles need to be extended to the greatest extent possible. Obviously, good health figures importantly into any asset maintenance equation.

Because of the above factors, current military doctrine calls for protecting the force from the hostile threats that are present in a military operation. Protecting the health of the force is an integral component of force protection. Its basic tenet is that preventing battlefield casualties is preferable to treating them. Force Health Protection is, therefore, a cornerstone to Force Protection.

Force Health Protection is founded on a national obligation to provide health care for our service personnel whether they are at home training in garrison or abroad dodging bullets. The Department of Defense's TRICARE program, which includes both the direct care system as well as care negotiated by managed care support contractors, serves as the venue for providing for medical readiness. A strong base of graduate and continuing health education supported by requirements-driven research are also essential elements of the health care system. Three basic pillars support health assuredness for deployed forces: promoting and sustaining wellness; preventing casualties, both from hostile action as well as from non-battle causes; and providing interventional health care.

Focusing on delivering to the war-fighting Commander-in-Chief (CINC) a health and fit force is the first step. Obviously, a healthy soldier, sailor, airman or marine requires less time away from his duty station on sick call. Therefore, achieving medial fitness by promoting health and wellness, intervening to treat health problems before sequellae render the member a medical casualty, and ensuring the work site is free from health hazards are of prime importance. Today's service member is often married with children, and so his or her ability to concentrate on their duties while away from their families in a hostile environment is enhanced by the knowledge that their families are receiving appropriate medical care when they need it.

Preventing casualties on the battlefield is the second pillar. In some respects, it can be considered an extension of wearing body armor or a Kevlar helmet. It begins with long-standing, basic preventive medicine doctrine to assure the health of the population. Immunizations and other countermeasures against biologic agents are also keys to survival. Being able to assess threats against health and document countermeasures employed are also vital elements. Stress, in its broadest definition, may well play a greater role than anticipated in adverse health effects from deployment, and so the ability to understand stressors and how to mitigate them becomes increasingly more important. Medical record keeping serves as an important tool not only in assuring that the best possible care is rendered but also in developing an understanding of emerging health issues. It is also essential to develop a longitudinal medical database to be used as a population-based research tool.

The third pillar, providing care on the battlefield, is the aspect of military medicine that heretofore has received the most attention. The overwhelming military victory in the Gulf War has the potential to lull military leaders into believing that future conflicts will be the same and not result in large numbers of battlefield casualties. While we all hope that is true, the ability to resuscitate, evacuate, and definitively care for the injured service man or woman represents a core competency for military medicine. The challenge to accomplish this in today's fast-paced, dynamic operational theater mandates new solutions, supported by research, to conventional medical problems. Training for battlefield medicine in the peacetime environment will require a greater reliance on computer generated devices upon which to train.

While a great many initiatives have been set in motion to realize the ambitious goals of a force health protection strategy, much remains yet to be accomplished.

PROTECTING THOSE WHO SERVE: STRATEGIES TO PROTECT DEPLOYED U.S. FORCES

John Moxley, M.D.

john.moxley@korn/ferry.com

The 670,000 service members deployed in 1990–1991 to Southwest Asia for Operations Desert Shield and Desert Storm (the Gulf War) were different from the troops deployed in previous similar operations: they were more ethnically diverse, there were more women and more parents, and more activated members of the Reserves and National Guard were uprooted from civilian jobs. The overwhelming victory that they achieved in the Gulf War has been shadowed by subsequent concerns about the long-term health status of those who served. Various constituencies, including a significant number of veterans, speculate that unidentified risk factors led to chronic, medically unexplained illnesses, and these constituencies challenge the depth of the military's commitment to protect the health of deployed troops.

Recognizing the seriousness of these concerns, the U.S. Department of Defense (DoD) has sought assistance over the past decade from numerous expert panels to examine these issues (DoD, 1994; National Institutes of Health Technology Workshop Panel, 1994; IOM, 1996a,b, 1997; Presidential Advisory Committee on Gulf War Veterans' Illnesses, 1996). Although DoD has generally concurred in the findings of these committees, few concrete changes have been made at the field level. The most important recommendations remain unimplemented, despite the compelling rationale for urgent action. A Presidential Review Directive for the National Science and Technology Council to develop an interagency plan to address health preparedness for future deployments led to a 1998 report titled *A National Obligation* (National Science and Technology Council, 1998). Like earlier reports, it outlines a comprehensive program that can be used to meet that obligation, but there has been little progress toward implementation of the program. Recently, the Medical Readiness Division, J-4, of the Joint Staff released a capstone document, *Force Health Protection*, which also describes a commendable vision for protecting deploying forces (The Joint Staff, Medical Readiness Division, 2000). The committee fears that the vision outlined in that report will meet the same fate as the other reports.

With the 10th anniversary of the Gulf War now here, the Committee on Strategies to Protect the Health of Deployed U.S. Forces has concluded that the implementation of the expert panels' recommendations and government-developed plans has been unacceptable. For example, medical encounters in theater are still not necessarily recorded in individuals' medical records, and the locations of service members during deployments are still not documented or archived for future use. In addition, environmental and medical hazards are not yet well integrated in the information provided to commanders. The committee believes that a major reason for this lack of progress is the fact that no single authority within DoD has been assigned responsibility for the implementation of the recommendations and plans. The committee believes, because of the complexity of the tasks involved and the overlapping areas of responsibility involved, that the single authority must rest with the Secretary of Defense.

The committee was charged with advising DoD on a strategy to protect the health of deployed U.S. forces. The committee has concluded that immediate action must be taken to accelerate implementation of these plans to demonstrate the importance that should be placed on protecting the health and well-being of service members. This report describes the challenges and recommends a strategy to better protect the health of deployed forces in the future. Many of the recommendations are restatements of recommendations that have been made before, recommendations that have not been implemented. Further delay could result in unnecessary risks to service members and could jeopardize the accomplishment of future missions. The committee recognizes the critical importance of integrated health risk assessment, improved medical surveillance, accurate troop location information, and exposure monitoring to force health protection. Failure to move briskly on these fronts will further erode the traditional trust between the service member and the leadership.

The four reports completed from the work of the first 2 years of this study (IOM, 1999; NRC, 2000a,c,d) provide detailed discussions and recommendations about areas in which actions are needed to protect the health of deployed forces. The committee has been informed by those reports and endorses the recommendations within them. In the present report, the committee describes six major strategies that address the areas identified from the earlier reports that demand further emphasis and require greater effort by DoD. The committee selected these strategies on the

basis of the contents of the four reports, briefings by the principal investigators of those reports, and input from members of the military and other experts in response to the four reports.

Strategy 1. Use a systematic process to prospectively evaluate non-battle-related risks associated with the activities and settings of deployments.

Strategy 2. Collect and manage environmental data and personnel location, biological samples, and activity data to facilitate analysis of deployment exposures and to support clinical care and public health activities.

Strategy 3. Develop the risk assessment, risk management, and risk communication skills of military leaders at all levels.

Strategy 4. Accelerate implementation of a health surveillance system that spans the service life cycle and that continues after separation from service.

Strategy 5. Implement strategies to address medically unexplained symptoms in populations that have deployed.

Strategy 6. Implement a joint computerized patient record and other automated record keeping that meets the information needs of those involved with individual care and military public health.

COMBAT AND OPERATIONAL STRESS CONTROL: PREVENTIVE INTERVENTIONS AND TREATMENT OF DEPLOYMENT RELATED STRESS

POC LTC E. Cameron Ritchie

Elspeth.Ritchie@ha.osd.mil

Executive Summary

All wars produce psychological, as well as physical, injury. Through the last century we have learned and implemented techniques to reduce those casualties. The DoD Directive on Combat Stress Control 6490.5 outlines those basic techniques and directs the Services to develop their own implementation plans. DoD/Health Affairs and the Services have been working towards improving prevention and treatment of combat and operational stress casualties. The USD (P&R) has mandated warfighter involvement in a working group to implement the principles of combat and operational stress control throughout the Services.

Combat Stress Reactions

Combat Stress Reactions are normal, predictable responses to abnormal, psychologically traumatic, sometimes terrifying and horrible experiences. The cornerstone of prevention is that relationships (bonding and cohesion) among unit members and of unit members for their leaders are protective. Such relationships also provide a source for healing psychological wounds. Therefore, primary prevention focuses on optimizing leadership, unit cohesion, and morale as protective factors.

Secondary prevention of combat stress reactions is short term, initiated in or as near to the Service member's unit as possible, as soon after symptoms appear, utilizing simple measures, such as reassurance, rest and replenishment. This treatment is offered with the expectation that the Service member's symptoms will resolve and the Service member will return to his/her unit quickly, where he/she is both needed and wanted. Tertiary prevention focuses on minimizing more severe psychological symptoms or disorders and long-term symptoms of combat experience when simple measures are ineffective. In every major war or conflict since World War I, military psychiatry has shown that this traditional approach to the management of combat stress greatly reduces risk of morbidity.

Recent Combat Stress Control Activities

Combat Stress Control is an ongoing and critically vital issue. Our CSC units have been very active in Somalia, Haiti, Kosovo, Bosnia, and on numerous other humanitarian missions. It is difficult to measure the impact of combat stress control units. However the Canadian Forces, which have not had an active Combat Stress Control policy, have experienced a high rate of PTSD among their peacekeepers following service in Rwanda and Croatia. They are now attempting to implement a program similar to ours.

Tools to combat long term psychiatric morbidity include: good unit morale, risk communication, stress inoculation, and critical event debriefings. Stress inoculation—the concept of preparing service members for sights, sounds and smells of combat and humanitarian missions—is an increasingly accepted tool. Information pamphlets on handling dead bodies and other stresses are available on the Army mental health website (Armymentalhealth.com) and from CHPPM.

Inspector General's Report

In February 1996, the Department of Defense (DoD) Inspector General's office published Report No. 96-079, "Evaluation Report on the Management of Combat Stress Control in the Department of Defense." The report made five recommendations:

1) That the Assistant Secretary of Defense for Health Affairs (ASD(HA)), the Joint Staff, the Defense Medical Standardization Board, the Military Departments and the Defense Modeling and Simulation Office coordinate and continue activities to ensure that the medical planning programs used by the Commanders in Chief of the Unified Commands and Service Secretaries incorporate fully combat stress casualty estimates,
2) That ASD (HA) assume responsibility for policy development and coordination within DoD,
3) That the Joint Staff, in coordination with ASD (HA) and the Military Departments, incorporate combat stress management guidance into joint doctrine,
4) That ASD(HA) issue DoD policy requiring the Military Departments to develop comprehensive combat stress control programs,

5) That the Military Services provide training in combat stress control to all Service members, the content and level of such training geared to the branch, rank and level of responsibility of the Service member.

The DoD Directive 6490.5, "Combat Stress Control" was signed in February of 1999. It mandates that:

1) CSC policies shall be implemented throughout the department of defense;
2) Service CSC consultants shall meet periodically;
3) Leadership aspects of combat stress prevention shall be emphasized;
4) CSC units shall train with operational organizations;
5) BICEPS principles (Brevity, Immediacy, Centrality, Expectancy, Proximity, Simplicity)
6) Members experiencing CSRs shall be managed within the unit;
7) Misconduct be handled through UCMJ; and
8) CSR casualty rates be collected discretely from neuropsychiatric and DNBI data.

The Defense Medical Readiness Training Institute (DMRTI)

The DMRTI coordinated tri-service meetings during 1999 and 2000 concerning implementation of the DoD. Pre- and post- deployment screening and other metrics are being developed. The training and implementation plans focus on who receives training, the format and quantity of that information, and how to incorporate the principles into practice.

Service Specific Implementation Plans were formulated in 1999. However these plans were awaiting the results of the DMRTI meetings and the "Leaders and Operational Stress" conference.

Leaders And Operational Stress Conference

This conference was co-sponsored by JCS, OSAGWI and HA. The "Leaders and Operational Stress" Conference was held June 00 at Ft. McNair. The objectives of the conference were: to initiate a continuing dialogue between the operational, medical and religious communities; to ensure that Service policies implementing the DoDD are operationally functional; and to identify assets and training for Command.

There were keynote speakers from all the services, Service panels and a Hotwash session. The content was targeted towards the warfighting community. There were over 250 attendees from all five Services, including over 25 active duty and retired officers of flag rank.

Current Status

On September 22nd, 2000 a meeting was held between the USDP&R, OASD/Health Affairs, OSAGWI, and AFCB to discuss the next steps. Dr. Rostker plans to send each Service Chief a memorandum asking for warfighter participation in a working group to implement training in and knowledge of combat/operational stress control along the line.

The DMRTI met again on October 25th to finalize their recommendations in the following areas: 1) definitions of combat and operational stress reactions vs psychiatric disorders; 2) the best methods of assessing individual and unit readiness; 3) training modules for medical personnel; and 4) to finish the gap analysis of training among medical personnel. This information will be available to the line working group.

Key Problems

Line "buy-in" is an ongoing problem. This has to be an issue that the line and personnel communities support and resource. Adequate education must take place at appropriate levels. This education should be supplemented by information available both in handouts and over the web.

THE RECRUIT ASSESSMENT PROGRAM: A PROGRAM TO COLLECT COMPREHENSIVE BASELINE HEALTH DATA FROM US MILITARY PERSONNEL

CAPT Kenneth C. Hyams, MC, USN

Epidemiology Department, Naval Medical Research Center, Silver Spring, MD

hyamsk@nmrc.navy.mil

Abstract

Pilot testing has begun on the *Recruit Assessment Program* (RAP). The RAP is a proposed DoD program for the routine collection of baseline demographic, medical, psychosocial, occupational, and health risk factor data from all US military personnel at entry into military service. As planned, this information will be maintained in a computerized database, which will be accessible by DoD and Department of Veterans Affairs' (VA) clinicians and preventive medicine personnel on a routine and confidential basis. If pilot testing is successful and the RAP is instituted, it will be the first building block of an electronic medical record and will provide several important functions within the DoD and VA, including automating enrollment into the military health care system, improving patient care and preventive medicine efforts, and providing critical data for investigations of health problems among military personnel and veterans. Use of a self-completed, scannable, paper-and-pencil questionnaire at the time of accession was determined to be the most practical, initial approach for collecting baseline health data. A questionnaire that can be accurately completed by recruits within approximately one hour is being developed and tested. If the feasibility of the RAP is demonstrated and the program implemented throughout DoD, it will provide a significant improvement in the military medical record system. For the first time, DoD and VA physicians, public health officers, and researchers will have access to comprehensive, baseline health status data.

THE MILLENNIUM COHORT STUDY AND OTHER NEW RESEARCH INITIATIVES AT THE DOD CENTER FOR DEPLOYMENT HEALTH RESEARCH

Gregory C. Gray, Ph.D.

DoD Center for Deployment Health Research

The DoD Center for Deployment Health is conducting a number of new research studies which will serve veterans and policy makers by providing important data regarding health behaviors, healthcare utilization, and the impact military service, particularly deployments, has upon veterans' health.

The *Millennium Cohort Study* is a probability-based, cross-sectional sample of 100,000 military personnel (as of October 2000) who will be followed prospectively by postal surveys every three years over a 21-year period. The 100,000 persons will be comprised of 30,000 veterans who have been deployed to Southwest Asia, Bosnia, or Kosovo since August 1997, and 70,000 veterans who have not been deployed to these conflicts. In October 2004 and October 2007, 20,000 new military personnel will be added to the cohort. The total of 140,000 veterans will be followed until the year 2022.

The primary objective of this study is to compare change in health status between deployed and nondeployed personnel and the adjusted incidence rates of chronic disease between cohorts. Secondary objectives include comparing the adjusted change in health between the cohorts as reflected by SF-36V scores and the Patient Health Questionnaire diagnostic assessment. This study will serve as a foundation upon which other routinely captured medical and deployment data may be added to answer future military questions regarding the health risks of military deployments, military occupations, and general military service.

The DoD Center is conducting DoD-wide surveillance for long-term adverse events, possibly associated with anthrax immunization of active duty US military service members. A central focus will be hospitalizations and birth defects. Concern about the potential long-term severe and/or permanent adverse effects of the vaccine appears to have been a leading reason for vaccine refusal, although long-term adverse effects of anthrax vaccine are neither known nor expected. We will periodically link anthrax vaccine data to DoD hospitalization and birth defect data to help ensure the earliest possible detection of any morbidity associations. This project adds to existing DoD-sponsored activities, and enhances force health protection by helping assure the early detection of as-yet-unknown potential long-term consequences of anthrax immunization.

There is anecdotal evidence that complementary and alternative medicine (CAM) use is increasing among US military populations. The *Use of Complementary & Alternative Medical Therapies among US Navy and Marine Corps Personnel* is a postal survey targeting 5,000 active-duty US Navy and Marine Corps personnel to gain better information about CAM use. The questionnaire will collect data regarding health habits, CAM use, belief in CAM efficacy, and reasons for seeking CAM therapies. Repeated mailings and incentives will be used to increase response rates. If an individual used one of the following treatments within the past year (1/1/00 – 12/31/00): acupuncture, homeopathy, herbal therapies, chiropractic, massage, exercise, high-dose megavitamins, spiritual healing, lifestyle diet, relaxation, imagery, energy healing, folk remedies, biofeedback, hypnosis, psychotherapy, and art/music therapy, he or she will be considered a CAM user. These data will be linked to existing medical records for each individual and this composite data will then be used to analyze patterns of healthcare utilization. CAM users will then be compared to nonusers for healthcare utilization outcomes and diagnoses.

TOWARD POPULATION-BASED POST-DEPLOYMENT CARE: DOD'S DEPLOYMENT HEALTH CLINICAL CENTER

Charles C. Engel, Jr., MD, MPH, Lieutenant Colonel, Medical Corps, US Army

Director, DoD Deployment Health Clinical Center
and Assistant Professor, Uniformed Services University

cengel@usuhs.mil or charles.engel@amedd.army.mil

Persistent war-related health concerns and medically unexplained physical symptoms (MUPS) among Gulf War veterans are a reminder of the challenges that health concerns and unexplained symptoms will pose for clinicians, scientists, and military forces in the future [1]. World War I veterans described debilitating physical symptoms and attributed them to chemical exposures [2]. Decades later, hundreds of thousands of Vietnam veterans sought evaluation for concerns related to agent-orange (dioxin) exposure [3]. Unexplained symptoms after government mandated vaccinations [4], peacekeeping in Croatia [5], and recent concerns about depleted uranium and a "Balkan War Syndrome," [6], must serve notice that we are in an age of zero societal risk tolerance, an omnipresent media, and advocacy driven public health debate.

Public dialogue regarding the health of military forces and veterans is essential, yet we must be mindful that scientific, media, and political debates may sometimes have harmful effects on the exact individuals the public aims to protect. When affected individuals receive exhaustive "no stone unturned" evaluations and simultaneously read and hear polarized public discussion, it can reinforce notions of covert scandal and conspiracy, amplify symptom-related psychosocial distress and disability, and lead to unnecessary utilization of health care and iatrogenesis [1].

Perhaps most damaging is the mistrust that can develop between veterans and their families who are highly concerned about their health and the government clinicians attempting to help them. This mistrust can drive symptomatic patients who are desperate for answers to try untested and potentially harmful therapies. Mistrust can also leave clinicians suspicious of veterans, skeptical of (if not even cynical about) the validity of their patients' reported exposures and symptoms. The resulting clinical dynamic may be viewed as a "contest" of sorts [7]. In this contest, the patient must battle to prove the validity of his or her symptoms, and the clinician resists offering validation until unequivocal biomedical evidence of disease is uncovered. This iatrogenic contest perpetuates disability, increases medical costs, and undermines opportunities to nurture the trusting clinician-patient relationship needed to embark on successful morbidity reduction strategies.

This contest as well as the troublesome biomedical tendency to formulate health concerns and MUPS as "non-problems" become the germ of a much bigger problem for the military and for public health. Anecdotes from veterans who feel their health concerns have been discounted do not go away with the passage of time. Instead these stories tend to grow, join, multiply, and infect progressively larger networks of concerned people. The result may be amplified population fears, erosion of public trust, and declining troop confidence that the government will ultimately protect them.

The best prevention in the face of this challenge is a comprehensive and caring approach to deployment-related health care including the care of health concerns and MUPS. The Department of Defense (DoD) has demonstrated a firm commitment in this direction with the creation of the Deployment Health Clinical Center (DHCC). DHCC is one of three DoD Centers for Deployment Health that will build upon past Army, Navy, and Air Force experience, expanding on current clinical, surveillance, and research efforts to improve the ability to identify, treat, and minimize or eliminate the short- and long-term adverse effects of military service on the physical and mental health of veterans. These centers reflect government commitment, and they also fulfill key recommendations outlined in the National Science and Technology Council's Presidential Review Directive 5. Presidential Review Directive 5 is a comprehensive interagency force health protection plan describing treatment, research, and surveillance efforts aimed at minimizing adverse health effects of deployment.

Deployment Health Clinical Center is critical to DoD efforts to achieve the clinical goals of Presidential Review Directive 5 and is committed to fostering and facilitating caring clinical approaches to post-deployment health care including the care of health concerns and MUPS. The DHCC mission includes responsibilities to (1) improve

primary and tertiary post-deployment health care, (2) develop a program of militarily relevant clinical research to include multi-center and health services research trials, and (3) develop clinician and patient education programs that explore and teach strategies for communicating with patients about MUPS, deployment-related risks, and health concerns. The success of DHCC will be measured against its capacity to improve deployment veterans' satisfaction with their care; improve health outcomes; complete clinical research resulting in merit-reviewed journal publications; and distribute timely information to clinicians and veterans on deployment-related health concerns and MUPS.

How can DHCC accomplish such a broad mission? The Institute of Medicine has endorsed the development of a stepped system of evidence-based rehabilitative care for the spectrum of concerns and MUPS that occur after military action [1]. A stepped care system, codified using clinical practice guidelines and tested empirically using a randomized multicenter controlled trial methodology, would entail pre-event and post-event preventive measures linked to a spectrum of health services including primary care, collaborative primary care, and intensive multimodal care [1]. Under this model, emphasis is placed on the use of automated information systems to match the optimal level of care to the chronicity and disability associated with each patient's MUPS and to carefully monitor populations of interest for appropriate health outcomes [1].

The roadmap to accomplishing this mission involves clinical experience, care-based efforts to build trust and communicate honest environmental risk information, personalized stepped-care strategies, clinical practice guidelines codifying those strategies, and continuous improvement efforts based on clinician education and research evaluating health systems. DHCC has an excellent experience base: it grew from the Gulf War Health Center, an organization with a 5-year history of successfully caring for veterans with deployment health concerns and MUPS [8]. DHCC is currently participating in a multi-agency effort involving the VA, and the US Army, Navy, and Air Force to develop and implement two sets of clinical practice guidelines, one to help government clinicians evaluate and manage post-deployment health issues and the other to do the same for MUPS. One consequence of these efforts has been the recognition that veterans and clinicians need sound and timely information regarding deployment-related exposures and deployment-specific health outcomes. A publicly accessible and dynamic DHCC web site will help accomplish this and is set to open in late March 2001. This web site represents an unprecedented development in government efforts to sustain an open dialogue with those it is charged with protecting and their clinicians regarding deployment-related exposures, diseases, health concerns, and MUPS. As these practice guidelines are implemented, DHCC will lead efforts to teach busy clinicians how to carry out the guidelines, and sensitize clinicians to the need for and approach to developing trust-based communications with veterans who are highly concerned about post-deployment health issues. DHCC is also participating in three major multicenter clinical trials with the VA's world-class clinical trial capability, the Cooperative Studies Program. Future DHCC initiatives include efforts to scientifically test the new clinical practice guidelines using controlled trial methods.

We can be certain that MUPS after military action or domestic crisis will continue to be the appropriate focus of intense societal debate. Indeed, the military stands for and is charged with protecting the right to a free and open debate regarding post-deployment health issues. The development and implementation of state-of-the-art post-deployment health care including the care of concerns and MUPS will ensure that post-deployment health care works efficiently, effectively, in the best interests of those who need services, and to the enhanced credibility of all military medicine.

References

1. Engel CC, Katon WJ: Population and need-based prevention of unexplained symptoms in the community. Strategies to Protect the Health of Deployed U.S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction, pp 173-212. Washington, DC, National Academy Press, 1999.
2. Straus SE: Bridging the gulf in war syndromes. Lancet 1999; 353:162-163.
3. Institute of Medicine: Veterans and Agent Orange: Update 1998, p 28. Washington, DC, National Academy Press, 1999.
4. Institute of Medicine: An assessment of the safety of the anthrax vaccine: a letter report. Washington, DC, 2000.
5. National Defence (Canada): Final Report: Board of Inquiry – Croatia. Canada, National Defence, 2000.
6. Rogers L: Ailing troops sue over Balkan war syndrome. The Sunday Times of London, News, 16 April 2000.
7. Hadler NM: If you have to prove you are ill, you can't get well. Spine 1996; 21(20):2397-2400.
8. Engel CC Jr, Roy M, Kayanan D, Ursano RJ: Multidisciplinary Treatment of Persistent Symptoms After Gulf War Service. *Military Medicine* 1998; 163(4):202-8

THE DEPARTMENT OF DEFENSE BIRTH DEFECTS REGISTRY

Margaret A. K. Ryan, MD, MPH

Department of Defense Center for Deployment Health Research,
Naval Health Research Center, San Diego, California

Introduction

The United States Department of Defense (DoD) is challenged with monitoring and protecting the health and wellbeing of all of its service members. The growing number of women on active duty and the diverse hazardous exposures associated with military service make reproductive health issues a special concern of DoD. Deployment experiences, especially the Gulf War, have served to highlight interest in reproductive health, and birth defects in particular. To address these concerns, the DoD Birth Defects Registry was established at the DoD Center for Deployment Health Research in 1998.

Surveillance Methodology

The population under surveillance by the DoD Birth Defects Registry includes all military beneficiary families. All live births that are financially sponsored by DoD, including births at military and civilian medical facilities, are captured. Birth defects among these infants are identified by ICD-9 coding of records from inpatient and outpatient encounters in the first year of life. The ICD-9 code range is consistent with state and national surveillance programs, such that the prevalence of birth defects in 45 major malformation categories may be calculated.

DoD Birth Defects Registry data analysts have established direct access to very large electronic databases to thoroughly capture all births and birth defect cases among DoD beneficiaries. Data sources include: Standard Inpatient Data Records system (military hospitalizations), Standard Ambulatory Data Records system (military outpatient care), and the Health Care Records System, that details inpatient and outpatient care provided at civilian facilities supported by DoD's TriCare insurance system.

To assess for potential under-reporting, over-reporting, or miscoding in the electronic surveillance system, active case finding has been established at one of the largest DoD health care facilities, the Naval Medical Center in San Diego. Registry staff review hospital and clinic records and contact clinicians to identify newly-diagnosed birth defects cases. Staff also review the full inpatient and outpatient records for suspected cases. Medical center data is compared to electronic data to verify the presence of birth defects, to validate ICD-9 coding, and to expand on diagnoses with the standardized coding used by state and national birth defects researchers.

Registry analysts also have access to very complete demographic and service-related information on active duty beneficiaries. Health care data may be linked to data from the Defense Enrollment Eligibility Reporting System and the Defense Manpower Data Center. Such data provide important profiles of military parents, including deployment and occupational exposure histories, that are relevant to birth defects research.

Results

More than 90,000 DoD-sponsored births have occurred annually since the DoD Birth Defects Registry was established. Sixty percent of births took place in military treatment facilities and 40% occurred in civilian facilities sponsored by TriCare.

Although the representation of women in the military is growing, less than 19% of DoD births identified the mother as an active duty member in the last two years. In all other cases, the mother was a dependent of a military member or other beneficiary. Average maternal age was 26 years, and ranged from 14 to 49 years. Among DoD births, the race of the sponsor was identified as Caucasian (70%), African American (20%), Asian (3%) or other race (7% of cases). Approximately 39% of births in the DoD registry are sponsored by the Army, 25% are Air Force-sponsored, 24% are Navy-sponsored, 11% are Marine Corps-sponsored, and 3% have Coast Guard or other sponsorship.

DoD-sponsored births take place in all 50 United States and the District of Columbia. This makes the registry data of great interest to state and national surveillance programs. California, Texas, and Virginia have the highest number of DoD-sponsored births, with more than 7,000 births in each of these states annually. It is important to note that nearly 8% of DoD births take place outside of the United States. In 1999, DoD-sponsored infants were born in 34 foreign countries; more than 2,400 were born in Germany and more than 2,000 were born in Japan.

The DoD Birth Defects Registry has identified 4% of all DoD-sponsored infants as having a birth defect diagnosed in the first year of life. This overall prevalence, and the prevalence of each specific defect category, has not been found to differ from data reported by U.S. state and national birth defects surveillance programs. Data from the registry are being linked to data on occupational and environmental exposures of concern to both the military and civilian public health communities.

Conclusion

Monitoring birth defects is consistent with the military's mission of providing the best health care and protection for its members. The DoD Birth Defects Registry also augments national public health goals to increase birth defects surveillance. The DoD is uniquely positioned to collect comprehensive health care data, and to assess occupational and environmental exposures in a geographically diverse population. DoD Birth Defects Registry information, along with data from other DoD research, will be vital for future public health studies, prevention efforts, and health policy decisions.

DEFENSE MEDICAL SURVEILLANCE SYSTEM (DMSS) AND THE ARMY MEDICAL SURVEILLANCE ACTIVITY

Mark Rubertone, M.D., MPH

U.S. Army Center for Health Promotion and Preventive Medicine

Medical surveillance is defined as the routine and systematic collection, analysis, interpretation, and reporting of population-based data for the purposes of detecting, characterizing, and countering threats to the health, fitness, and well being of populations. In military settings, medical surveillance is required to develop and maintain healthy, fit, and operationally effective forces and to ensure their "total protection" during training and operational missions.

The Army Medical Surveillance Activity (AMSA) was established in 1994 as part of the Directorate of Epidemiology and Disease Surveillance, U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM). The AMSA staff includes information systems specialists, database managers, programmers, analysts, statisticians, epidemiologists, preventive medicine physicians, and public health officers from each of the three Services. In March 1997, the Assistant Secretary of Defense for Health Affairs (ASD-HA) directed that the Army establish and operate a Defense Medical Surveillance System (DMSS) by transitioning the current capability of the Army Medical Surveillance System (AMSS). AMSA coordinated the development of and now operates the DMSS.

The Army Medical Surveillance Activity's (AMSA) main functions are to analyze, interpret, and disseminate information regarding the status, trends, and determinants of the health and fitness of America's Army and to identify and evaluate obstacles to medical readiness. AMSA is the central epidemiological resource for the Army providing regularly scheduled and customer-requested analyses and reports to policy makers, medical planners, and researchers. It identifies and evaluates obstacles to medical readiness by linking various databases that communicate information relevant to soldiers' experience that has the potential to affect soldiers' health.

The Defense Medical Surveillance System (DMSS) is the corporate executive information system for medical surveillance decision support in the EI/DS business area of the Military Health System (MHS). The DMSS receives and integrates standardized data from multiple individual Service and DoD sources worldwide (table 1). The "engine" of the DMSS is a continuously growing relational database of up-to-date and historical data related to medical events (e.g., hospitalizations, outpatient visits, reportable diseases, HIV results, health risk appraisals, immunizations, deaths), personal characteristics (e.g., rank, military occupation, demographic factors), and military experiences (e.g., deployments, assignments) of all Army, Navy, Air Force, and Marine servicemembers over their entire military careers. There are currently more than 150 million rows of data regarding more than 6.5 million servicemembers in the on-line DMSS database.

The Defense Medical Epidemiology Database (DMED) application provides authorized users worldwide (through the Internet) with real-time access to user-definable queries of a subset of data (non-privacy) contained within the DMSS.

The AMSA/DMSS produces data summaries, epidemiologic analyses, and special reports for policy makers, medical planners, health care practitioners, and researchers worldwide. The Medical Surveillance Monthly Report (MSMR) is the principal vehicle of AMSA/DMSS for the routine dissemination of medical surveillance information of broad interest. The MSMR publishes summaries of notifiable diseases, trends of special surveillance interest (e.g., deployment-related morbidity), and field reports of outbreaks and isolated cases with special public health or military operational significance. Current and previous issues of the MSMR are accessible from AMSA's home page (http://amsa.army.mil).

AMSA and the DMSS provides the sole link between medical surveillance data (e.g., personnel, military experience, medical outcomes) and specimens in the DoD Serum Repository. The DoD Serum Repository, the largest of its kind in the world, contains more than 26 million frozen archived serum specimens from members of all the military services.

Further information regarding the availability, use or interpretation of data contained in DMSS and DMED or access to specimens in the DoD Serum Repository may be directed to the staff at the AMSA (202) 782-0471 (DSN: 662). POC: LTC Mark Rubertone, MC, USA, Chief, Army Medical Surveillance Activity, US Army Center for Health Promotion and Preventive Medicine, (202) 782-0471 (DSN: 662), e-mail: "mark.rubertone@amedd.army.mil".

Table 1. Selected Data Tables Integrated within the Defense Medical Surveillance System (DMSS)*

Table	Source	Frequency	Rows	Services	Period of time
Person[1]	DMDC	Monthly	6.8M	All	1990 -- 2000
Demog[1]	DMDC	Monthly	59M	All	1990 -- 2000
MEPS	MEPCOM	Monthly	7.2M	All	1985 -- 2000
Deploy_PGW[2]	DMDC	Single	696K	All	1990 -- 1991
Deploy[3]	DMDC	Monthly	390K	All	1993 -- 2000
SIDR	CEIS	Monthly	1.8M	All	1990 -- 2000
SIDR_OJE	PASBA	Weekly	8.0K	All	1996 -- 2000
Deploy_Forms[4]	AMSA	Daily	141K	All	1996 -- 2000
SADR	CEIS	Monthly	35M	All	1996 -- 2000
SADR_SWA	DCII	Monthly	58K	All	1998 -- 2000
HIV_Tests[5]	Testing Labs	Weekly	25M	All	1985 -- 2000
Immunizations	DEERS	Monthly	10.2M	All	1980 -- 2000
DoDSR	DoDSR	Weekly	25.9M	All	1985 -- 2000
Casualty[6]	DIOR	Quarterly	20.8K	All	1985 -- 2000
HRA	CHPPM	Quarterly	798K	Army	1990 -- 2000
Reportable Events[7]	MTFs	Daily	61K	All	1994 -- 2000

* Last Updated: Aug-00

Notes:
1. Person / Demog contain all persons serving on active duty and in the reserve component
2. Deployment roster for Persian Gulf War
3. Deployment roster for major deployments since PGW
4. Health assessment questionnaires administered before / after major deployments
5. Data from mandatory HIV tests performed on DoD personnel and MEPS applicants
6. Casualty data on active duty deaths
7. As outlined in the Tri-Service required list of reportable events

Acronyms:
CEIS -- Corporate Executive Information System
CHPPM -- USA Center for Health Promotion and Preventive Medicine
DCII -- Desert Care II
DEERS -- Defense Enrolment Eligibility Reporting System
DIOR -- Directorate for Information, Operations and Reports
DMDC -- Defense Manpower Data Center
DoDSR -- Department of Defense Serum Repository
HRA -- Health Risk Appraisals
MEPS -- Military Entrance Processing Stations
MTF -- Military Treatment Facility
OJE -- Operation Joint Endeavor
PASBA -- Patient Administration Systems and Biostatistics Activity
SADR -- Standard Ambulatory Data Record
SIDR -- Standard In-Patient Data Record
SWA -- Southwest Asia