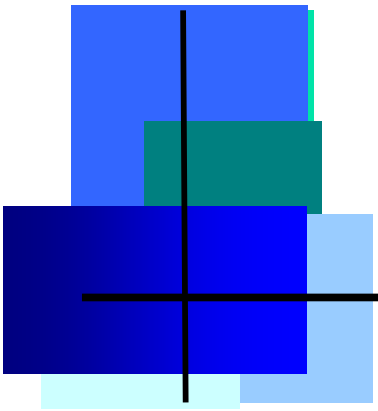
Department of Veterans Affairs

ANNUAL REPORT TO CONGRESS

Federally Sponsored Research on Gulf War Veterans' Illnesses for 2008

July 2009

Deployment Health Working Group Research Subcommittee



Annual Report to Congress – 2008

Federally Sponsored Research on Gulf War Veterans' Illnesses for 2008

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EXECUTIVE SUMMARY

I. INTRODUCTION

Section 707 of Public Law 102-585, as amended by section 104 of Public Law 105-368, requires that an annual report be submitted to the Senate and House Veterans' Affairs Committees on the results, status, and priorities of research activities related to the health consequences of military service in the Gulf War (Operations Desert Shield and Desert Storm; August 2, 1990 – July 31, 1991). The Research Subcommittee of the interagency Deployment Health Working Group (DHWG) prepared this *2008 Annual Report to Congress*, which is the fifteenth report on Federal research and research activities. The DHWG tracks all federally funded research projects related to Gulf War Veterans' illnesses (GWVI).

As in previous *Annual Reports to Congress*, the material presented is divided into 5 sections. Section I is an introduction; Section II summarizes the research priorities and organization of the Federal Gulf War (GW) research portfolio; Section III highlights and summarizes research progress published since the last *Annual Report*; Section IV summarizes Federal funding trends for GW research during the 10-year period from fiscal year (FY) 1999 through FY 2008; and Section V highlights new research projects and initiatives.

II. RESEARCH PRIORITIES

The research priorities remain unchanged from last year. The 19 Research Topics (2 of the original 21 topics were eliminated in the 2006 Annual Report) are grouped into five major Research Focus Areas. These Research Focus Areas are used to organize Sections III and V, as well as Appendix B (Project Listing by Research Focus Area). In November 2005, at the request of the Secretary of Veterans Affairs (VA), the VA Office of Research and Development (ORD) developed a set of criteria for inclusion of VA-funded projects in the GW research portfolio and then evaluated the entire VA research portfolio for projects meeting those criteria. The criteria used as the basis for the review are presented in Section II.

III. PUBLISHED RESULTS AND STATUS OF THE FIELD IN 2008

Section III provides brief summaries of research articles on the health problems of GW Veterans published during calendar year 2008 or in 2007 after the previous Annual Report was submitted. Research results are grouped according to the five Research Focus Areas used to organize the 19 Research Topics (see Section II): Brain and Nervous System Function, Environmental Toxicology, Immune Function, Reproductive Health, and Symptoms and General Health Status. In this section, published research results are described followed by specific study abstracts taken from PubMed.

IV. RESEARCH FUNDING TRENDS

From FY 1992 through FY 2008 the Departments of Veterans Affairs (VA), Defense (DoD), and Health and Human Services (HHS) funded 347 distinct projects related to health problems affecting GW Veterans. The scope of the Federal research portfolio is broad, from small pilot studies to large-scale epidemiology studies involving large populations and major center-based research programs. Federal funding for research on GWVI totaled approximately $273 million for the period from FY 1999 through FY 2008. As of September 30, 2008, 288 projects (83 percent of the 347 projects) were completed, and 59 projects (17 percent) were new or ongoing.

V. NEW RESEARCH PROJECTS AND INITIATIVES

VA funded 2 new projects in FY 2008 focused on Brain and Nervous System Function.

I. INTRODUCTION

The Secretary of Veterans Affairs (VA) is required by section 707 of Public Law 102-585, as amended by section 104 of Public Law 105-368, to submit an annual report on the results, status, and priorities of research activities related to the health consequences of military service in the Gulf War to the Senate and House Committees on Veterans' Affairs. The Research Subcommittee of the interagency Deployment Health Working Group (DHWG) prepared this *Annual Report to Congress for 2008*, which is the fifteenth report on research and research activities (DHWG, 2004; DHWG, 2005; DHWG, 2006a; DHWG, 2006b; DHWG, 2007; DHWG, 2008; MVHCB, 2001; MVHCB, 2002; Pastula et al., 2008; PGVCB, 1995; PGVCB, 1996a; PGVCB, 1996b; PGVCB, 1997; PGVCB, 1998; PGVCB, 1999; PGVCB, 2001). The DHWG tracks all federally funded research projects related to GWVI.

As in previous *Annual Reports to Congress*, the material presented is divided into five sections. Section I is an introduction. Section II summarizes the research priorities and organization of the Federal GW research portfolio. Section III highlights and summarizes published research progress since the last *Annual Report*. Section IV summarizes Federal funding trends for GW research during the 10-year period from FY 1999 through FY 2008. Section V highlights new research projects and initiatives since the last *Annual Report*.

II. RESEARCH PRIORITIES

A. Nineteen Research Topics

The Persian Gulf Veterans Coordinating Board (PGVCB) was created in 1994 to coordinate research from VA, DoD, and HHS on GWVI. In 1995, the PGVCB devised a contextual framework for the results of completed and ongoing studies and also to develop an approach for the interpretation of research results. To that end, the PGVCB identified 19 major research questions and subsequently added two additional questions in 1996 (PGVCB, 1996a), to bring the total to 21. The comprehensive GW research portfolio has addressed each of these 21 questions, and relevant results have been published on each one. The Military and Veterans Health Coordinating Board (MVHCB), the successor organization to the PGVCB, conducted a comprehensive assessment of the progress made on each of these 21 questions in the *Annual Report to Congress for 2000*. The Research Subcommittee of the DHWG, which was established to address a broader range of deployment health issues, reviewed the 21 questions and replaced them with a corresponding list of 21 Research Topics for the *Annual Report to Congress for 2004* (DHWG, 2006a).

The original list of 21 questions has been reduced to 19. Based on the Institute of Medicine of the National Academies (IOM) review of the scientific literature on infectious diseases (Institute of Medicine, 2006b) and the state of our current scientific knowledge, the conclusion was reached in the 2006 Annual Report (DHWG, 2007) that there is no rationale to continue inclusion of infectious diseases as an area of research that will provide answers to the causes or cure for these symptoms. Questions 2 and 19 have, therefore, been removed from the original list of 21 Questions and the third Research Focus Area has been refocused from Immune Function and Infectious Diseases to just Immune Function. Projects originally identified as "GW research" under these two questions will continue to be listed in Appendices A and B, but no funding amounts will be shown for FY 2007 or beyond.

Similarly, PTSD-related projects that were originally included in the Federal GW research portfolio were closed as of FY2007 (i.e., no funds listed in Appendix C) if they did not directly study a population of ill GW Veterans or were not investigating treatments that may prove beneficial for ill GW Veterans.

The IOM report reviewing the available literature on Amyotrophic Lateral Sclerosis (ALS) in Veterans (Institute of Medicine, 2006a) concluded there is limited and suggestive evidence of an association between military service and later development of ALS. This strengthens the decision to include ALS as a relevant topic in the Federal portfolio of GW research (DHWG, 2006b). ALS projects included in the GW portfolio are primarily focused on epidemiologic studies in GW Veterans and the development of new methodologies to identify and/or treat ALS.

The organization of the remaining 19 Research Topics into five major categories is described in Section B below.

B. Research Portfolio Descriptors

VA maintains a research database of federally sponsored research on GWVI. This includes research conducted by Federal scientists, as well as that by non-Federal scientists supported by Federal research funds through grants, contracts, and cooperative agreements. It is not possible to accurately track research efforts that fall within the private sector or otherwise outside of the purview of the Federal government.

Nonetheless, the Research Subcommittee of the DHWG attempts to stay abreast of all research relevant to GWVI. This is accomplished by monitoring peer-reviewed published scientific literature, attending scientific meetings, and even using newspaper reports and personal accounts of researchers.

Appendix A lists the projects that VA, DoD, and HHS have funded to date. Research projects are grouped according to the department that is responsible for funding. Dual-funded projects are listed under both departments.

Appendix B lists all federally funded GW research projects, regardless of the agency providing the funding. Three descriptors are used to categorize each funded project.

The first descriptor is the primary **Research Focus Area** of the project. The five Research Focus Areas are also used to organize the 19 Research Topics (see Section A, above).

- Brain and Nervous System Function (e.g., studies on neurological or psychological deficits and/or alterations)
  - Organic neuropsychological and neurological deficits (original Question 16)
  - Psychological symptoms and/or diagnoses (original Question 18)
- Environmental Toxicology (e.g., studies focused on specific environmental exposures such as pesticides, oil well fires, jet fuel, vaccines, medical prophylactic agents, etc.)
  - Petroleum products and combustion products (original Question 3)
  - Occupational/environmental hazards (original Question 4)
  - Organophosphorus nerve agent and/or sulfur mustard from bombing at Muhammadiyat or weapons bunker at Khamisiyah (original Question 5)
  - Chemical agents, other than at Khamisiyah (original Question 6)
  - Pyridostigmine bromide (PB) and other medical prophylaxes (e.g., vaccines and anti-malarials) (original Question 7)
  - Psychophysiological stressors (original Question 8)
  - Short term, low level exposures to pyridostigmine bromide, N,N-diethyl-m-toluamide (DEET), or permethrin, alone or in combination as a cause of short-term and/or long-term neurological effects (original Question 17)
- Immune Function (e.g., studies on alterations in immune function or host defenses)
  - Altered immune function or host defense (original Question 10)
- Reproductive Health (e.g., studies on sexual and/or reproductive dysfunction)
  - Birth defects in offspring (original Question 11)
  - Lower reproductive success (original Question 12)
  - Sexual dysfunction (original Question 13)
- Symptoms and General Health (e.g., studies on mortality, pulmonary disease, cancer, chronic multisymptom illnesses, etc.)
  - Increased prevalence or severity of symptoms and/or illnesses (original Question 1)
  - Nonspecific symptoms and symptom complexes (e.g., chronic multisymptom illnesses) (original Question 9)
  - Changes in lung function or airway reactivity (original Question 14)
  - Smaller baseline lung function or greater degree of nonspecific airway reactivity (original Question 15)
  - Development of cancers of any type (original Question 20)
  - Mortality rates (original Question 21)

Secondary and/or tertiary Research Focus Areas from the above list may also be assigned. Two additional Research Focus Areas may be used for secondary and tertiary assignments. This permits accounting for projects that cover multiple focus areas.

- Chemical weapons (e.g., sarin, sulfur mustard, etc.)
- Pyridostigmine bromide and other medical prophylaxes (e.g., vaccines, pyridostigmine bromide, antimalarials, etc)

The second descriptor is the **Project Focus**, categorized as follows:

- Diagnosis: studies that will improve the ability to diagnose previously unexplained conditions, or to better refine diagnoses with new tools
- Exposure: studies that examine individual exposures and/or interactions of exposures (chemical, biological, pharmacological, physiological, etc.)
- Interactions: interactions of combined exposures (chemical, biological, pharmacological, physiological, etc.)
- Prevention: studies that will produce knowledge that could lead to disease prevention strategies
- Symptoms: prevalence and risk factors for symptoms and alterations in general health status
- Treatment: development or testing of new therapies

Each project is assigned up to three Project Focus areas as categorical descriptors. This allows accounting for projects that cover multiple focus areas. For example, a project on the neurophysiological effects of exposure to sarin in animals would have a focus on the brain and nervous system, and a focus on chemical weapons. The number of focus areas (between one and three) assigned to a project depends on the project itself.

The third descriptor for each project is **Research Type**. Each research project on GWVI uses a method of approach to test a specific research hypothesis. Although precise categorization of research types can be difficult because of overlapping methodologies, research projects can be divided into the following general types:

MECHANISTIC: Research into underlying mechanisms of diseases and illnesses using in vitro and in vivo models.

CLINICAL: Application of an intervention, such as in a controlled drug trial, or use of methodologies such as case-control studies to define risk factors for disease.

EPIDEMIOLOGY: Study of the distribution and determinants of disease in human populations. It includes population-based studies focused on outcomes such as mortality, symptoms, hospitalizations, etc., using devices such as postal surveys, telephone interviews, and reviews of medical records.

DEVELOPMENT: In addition to tracking research on GWVI, the DHWG also tracks development activities. In general, development is the systematic use of the knowledge or understanding gained from research directed toward the production of materials; devices; systems; or methods, including design, development, and improvement of prototypes and new processes. Within the context of GWVI, the DHWG categorizes activities as development as an activity that satisfies the general definition of development described above, and is directed toward new biologically based prevention, intervention, and treatment measures.

The research database on GWVI catalogs only research and development activities that either directly involve GW Veterans or answer specific questions about risk factors. An example of the latter is a research project using animal models to determine health effects of low-level chemical warfare agents. The database does not account for the vast accumulated knowledge derived from the Nation's investment in more generalized biomedical research over the past 50 years.

C. Portfolio Criteria

In November 2005, at the request of the Secretary of VA, the VA Office of Research and Development (ORD) developed a set of criteria for inclusion of VA-funded projects in the GW research portfolio. The criteria and relevant references from that analysis are presented below. These criteria are now routinely used to identify relevant research projects. New projects selected for funding must meet these criteria and are presented in Section V.

1. Studies of chronic multisymptom illnesses (CMI) affecting GW Veterans, including case definitions for CMI in GW Veterans and the general population.
    a) Case definitions of multisymptom illnesses affecting GW Veterans
    (Fukuda et al., 1998; Haley et al., 1997a; Haley et al., 1997b; Haley et al., 2002; Wolfe et al., 2002)
    b) Chronic fatigue syndrome
    (Dunphy et al., 2003; Eisen et al., 2005; Gray et al., 2002; The Iowa Persian Gulf Study Group, 1997; Unwin et al., 1999)
    c) Fibromyalgia
    (Eisen et al., 2005; The Iowa Persian Gulf Study Group, 1997)
    d) Irritable bowel syndrome
    (Dunphy et al., 2003; Gray et al., 2002)
    e) Multiple chemical sensitivity (MCS)
    (Fiedler et al., 2004; Gray et al., 2002)

2. Conditions and/or symptoms occurring with higher prevalence in GW Veterans
    a) Fatigue
    (CDC, 1995; Coker et al., 1999; Doebbeling et al., 2000; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; The Iowa Persian Gulf Study Group, 1997; Unwin et al., 1999; Wolfe et al., 2002)
    b) Joint and muscle pain
    (CDC, 1995; Coker et al., 1999; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997a; Haley et al., 1997b; Haley, 2003; Kang et al., 2000; Pierce, 1997; Proctor et al., 1998; The Iowa Persian Gulf Study Group, 1997; Wolfe et al., 2002)
    c) Gastrointestinal complaints (dyspepsia, gastritis, diarrhea, etc.)
    (Blanchard et al., 2006; CDC, 1995; Coker et al., 1999; Eisen et al., 2005; Fukuda et al., 1998; Gray et al., 2002; Haley et al., 1997b; Kang et al., 2000; Proctor et al., 1998)
    d) Cognitive dysfunction (memory, attention, etc.)
    (CDC, 1995; Coker et al., 1999; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Proctor et al., 1998; The Iowa Persian Gulf Study Group, 1997; Wolfe et al., 2002)
    e) Sleep disturbances
    (CDC, 1995; Coker et al., 1999; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Pierce, 1997; Proctor et al., 1998; Unwin et al., 1999; Wolfe et al., 2002)
    f) Central Nervous System disorders (ALS, glioblastoma, imaging studies, etc.) Headaches
    (Bullman et al., 2005; Haley, 2003; Horner et al., 2003; Weisskopf et al., 2005)
    g) Headaches
    (CDC, 1995; Coker et al., 1999; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Proctor et al., 1998; Unwin et al., 1999; Wolfe et al., 2002)
    h) Dermatologic conditions
    (CDC, 1995; Coker et al., 1999; Eisen et al., 2005; Fukuda et al., 1998; Gray et al., 1999; Kang et al., 2000; Knoke et al., 2000; Pierce, 1997; Proctor et al., 1998; Wolfe et al., 2002)
3. Long-term health effects of potentially hazardous substances, alone and in combination, to which GW Veterans may have been exposed to during deployment.
    a) Pyridostigmine bromide
    b) DEET
    c) Permethrin
    d) Oil well fire smoke
    e) Petroleum products (e.g., jet fuels) and combustion products
    f) Multiple vaccinations and other medical prophylaxes

4. Other topics from the 19 Topics forming the framework for the *Annual Report to Congress on Federally Sponsored Research on GW Veterans' Illnesses:*

   a) Altered immune function and/or host defense
   b) Physiological responses to biological stress
   c) Sexual and/or reproductive dysfunction

III. PUBLISHED RESULTS AND STATUS OF THE FIELD IN 2008

Since the last Annual Report numerous research studies have provided new and detailed information on the health problems of GW Veterans. A PubMed search retrieved 69 relevant articles published in English in calendar year 2008 or in 2007 after the last Annual Report was submitted. These articles include federally and non-federally funded research, as well as international research. This section provides brief highlights of the published research divided into the five Research Focus Areas described in Section II. B. above, followed by the PubMed abstracts.

A. Brain and Nervous System Function

Studies relevant to GW Veterans and their family were reviewed and are presented in this section if they provided information about the brain and nervous system, including amyotrophic lateral sclerosis (ALS), depression, and posttraumatic stress disorders.

Amyotrophic Lateral Sclerosis (ALS)

Prompted by recent reports of a potentially increased risk of ALS among Veterans deployed to the Persian Gulf in 1990-1991, the Department of Veterans Affairs (DVA) Cooperative Studies Program (CSP) has established a National Registry of Veterans with ALS. During an enrollment period of 4 ½ years, 2,400 Veterans had consented to participate in the registry, of whom 2,068 were included after medical record review that confirmed the diagnosis and 1,573 consented to participate in the DNA bank (Allen et al., 2008). Fourteen studies have been approved to use the registry data for epidemiological, observational and interventional protocols. In addition to potentially leading to important new discoveries about ALS, the Registry has proven to be a successful model for identifying large numbers of patients with a relatively rare disease and enrolling them into multiple studies, including genetic protocols. One of the ALS protocols is the Genes and Environmental Exposures in Veterans with ALS study (GENEVA), a case-control study presently enrolling cases from the DVA ALS Registry and a representative sample of Veteran controls to evaluate the joint contributions of genetic susceptibility and environmental exposures to the risk of sporadic ALS (Schmidt et al., 2008), which represents 90-95 percent of ALS cases. The study has, thus far, recruited 537 ALS subjects and 292 controls.

A systematic review of the literature was conducted using MEDLINE, EMBASE, CINAHL, and Cochrane databases to identify occupational and environmental factors that may contribute to the risk of developing sporadic ALS (Sutedja et al., 2008). Of 3773 potentially relevant studies, 51 were initially included and 12 of these provided risk estimates for individual occupations. While there were methodological limitations and data could not be pooled due to the heterogeneity of study methods, several candidate occupations emerged: veterinarians and other health workers, athletes, hairdressers, power-production plant, electrical and military workers. However, additional studies with standardized assessment of occupation are needed to provide a more definitive answer about exogenous risk factors of ALS.

In a study of the clinical pattern of ALS among Veterans 1085 Veterans in the National Registry of Veterans with ALS were evaluated for deployment history and the duration of ventilator-free survival from date of first diagnosis (Pastula et al., 2008). In this unique cohort of Veterans with ALS (98 percent male, 94 percent white, 95 percent sporadic and 76 percent extremity-onset) traditional factors of reduced survival remained important. However, older age at diagnosis, non-extremity site of onset, and past deployment to Vietnam were all associated with shortened survival. In a fourth study, data from the 2.5 million military personnel who were on active duty during the 1991 Gulf War were analyzed (Horner et al., 2008). Among those Veterans, 124 cases of ALS were identified for the decade after the 1991 War, with the highest incidence observed in 1996, declining thereafter. Forty-eight cases of ALS occurred in Veterans deployed to the Persian Gulf region. Among the Veterans not deployed to the Gulf region, the level of risk remained constant during the same time period (1991-2001).

Two studies examined risk factors that might indicate an etiological origin of ALS. In one study, specific geographic locations of troop units within the 1991 GW theatre were associated with an increased risk for the subsequent development of ALS among members of those units (Miranda et al., 2008). These locations might represent the logical starting points in the search for potential etiologic factors of ALS among GW Veterans. However, for locations where the relative odds of subsequently developing ALS were among the highest, specific risk factors, whether environmental or occupationally related, have not been identified. In the other study, which reviewed the literature on epidemiology, no etiological factor leading to ALS was found (Matias-Guiu et al., 2008). However, exposure to heavy metal appeared to be consistently linked to the disease. Furthermore, the authors suggested that greater physical activity or increased frequency in special situations such as deployment in the first GW could be a precipitating factor.

PTSD

Three studies examined the prevalence of PTSD among different Veteran groups and services, and its social impact. In the first study, the characteristics and mental health needs of Veterans seeking treatment for PTSD were compared among those who served in Iraq/Afghanistan, the first GW, and the Vietnam War (Fontana and Rosenheck, 2008). As compared to Vietnam Veterans, Iraq/Afghanistan and first GW Veterans were more likely to be younger, female, single, and working. They were also less likely to be incarcerated or to report exposure to atrocities in the military. Furthermore, Veterans of the recent wars who sought treatment for PTSD were more likely to have intact social functioning, which might offer a window of opportunity for treatment interventions based on available social assets. In the second study, PTSD-like symptoms were evaluated among 311 male or female GW Veterans in National Guards/Reserve or in active duty (Vogt et al., 2008). The authors found that deployment stressors generally exerted more negative impacts on active duty women and National Guard/Reserve men than on other groups. In the third study, 1,512 Veterans of Operation Desert Storm were evaluated for PTSD symptoms (Taft et al., 2008) and family adjustment. The authors reported that higher combat exposure was associated with higher PTSD symptoms in both male and female Veterans. Female Veterans, in particular, experienced a significant direct negative association between combat exposure and family adjustment, including symptoms of withdrawal/numbing or arousal/lack of control.

Three studies examined the effect of PTSD among Kuwaiti GW Veterans, their wives and their children. The results from these studies may pertain to US Veterans. In the first study, four groups of Kuwaiti military men, 50 in each group, were recruited that represented the range of increasing exposure to war trauma, (1) retired before the War (2) served but not in a combat role (3) involved in combat, and (4) prisoners of war (Al-Turkait and Ohaeri, 2008b). The subjects were interviewed once, 6 years after the War, and evaluated for the severity of impact of event, depression, anxiety, self-esteem and locus of control. The authors found that 63 subjects met the criteria for PTSD with the highest proportion (48 percent) in the POW group. Avoidance symptoms, low self esteem and external locus of control were all most pronounced in the POWs with PTSD. Furthermore, self esteem was the only covariate of PTSD scores, while locus of control was a significant covariate for anxiety. The results suggested that intervention strategies should be focused on restoring self esteem and locus of control. In the second study, 176 wives of the subjects in the first study were evaluated for PTSD and family adjustment. The data were then correlated with the amount of exposure to war trauma of their husbands (Al-Turkait and Ohaeri, 2008a). The authors reported that 50 (28.4 percent) women met criteria for probable PTSD. The prevalence was significantly associated with the women's presence in Kuwait and husbands' combat exposure, but not with husbands' PTSD status. Wives' PTSD could be predicted by their depression/anxiety scores. The findings supported the salience of effective social support, and the need for to empower women through psychosocial interventions. In the third study, 489 children (250 male, 239 female) of 166 Kuwaiti military families were evaluated for the severity of anxiety, depression, deviant behavior and poor family adjustment (Al-Turkait and Ohaeri, 2008c). The authors reported that children of POWs tended to have higher anxiety, depression, and abnormal behavior scores. Those whose fathers had PTSD had significantly higher depression scores. However, children of fathers with both PTSD and POW status (N = 43) did not have significantly different outcome scores than the other father PTSD/combat status groups. Mothers' PTSD, anxiety, depression and social status were significantly associated with all the child outcome variables. The mothers' anxiety level was the most important predictor of the child's outcome. The primacy of the maternal influence has implications for interventions to improve the psychological functioning of children in such families.

B. Environmental Toxicology

Environmental agents potentially toxic to GW Veterans in theater were the topics of numerous scientific reports in 2008. These agents can be divided into 4 groups: (1) depleted uranium (DU), which is used in armor-piercing munitions; (2) nerve agents (e.g., sarin) and anti-nerve agents (e.g. pyridostigmine bromide); (3) insecticides (e.g., permethrin, chlorpyrifos) and insecticide repellents (e.g., Deet); and (4) jet fuel and its component hydrocarbons.

Depleted Uranium (DU)

New methods for measuring uranium were reported in 2008. A new sensitive mass spectrometric technique was developed and shown capable of measuring urinary DU 20 year after exposure to sufficient quantities of inhaled DU (Parrish et al., 2008). Sector field inductively coupled plasma-mass spectrometry methodology was developed to measure uranium in urine. This methodology was used to determine urinary uranium in military personal involved in the 2003 invasion of Iraq. There was no significant difference in urinary uranium between 4 different groups with potentially different levels of exposure to DU. The authors concluded that any uptake of DU among these participants would be very unlikely to have any health implications (Bland et al., 2007). An algorithm was developed that uses the amount of daily DU excreted in the urine to estimate the radiation dose received from DU material (Li et al., 2008). A mathematical model was developed that estimated the risks of DU-induced leukemia or birth defects in GW Veterans. It was estimated that his risk was far too small to have any observable changes in these end-points (Marshall, 2008). This model also predicted that only a few (approx. 5) Veterans in vehicles accidentally targeted by US tanks would receive significant exposure to DU to increase their radiation-induced fatal cancer lifetime risks by only 1.4 percent.

Veterans with various pathologies who had been exposed to DU munitions during the 1990-1991 Gulf War, Bosnia conflict, and Kosovo conflict had their urine analyzed for uranium content. None of the urine samples contained abnormal levels of uranium, which suggest that the pathologies seen in the Veterans were not related to exposure to DU (Cazoulat et al., 2008). Urinary uranium was determined in British personnel that served in Iraq during 2003. While there were some differences between officers and other ranks and between services, the levels recorded were within the normal range (Miller et al., 2008). There was a high degree of agreement between electronic occupation data, self-reported occupations data and self-reported exposure to various environmental toxins (e.g., DU, pesticides) for active duty and Reserve/Guard female participates in the Millennium Cohort (Smith et al., 2007b). A longitudinal study of GW Veterans showed that those with combat exposure or those with combat stress were more likely to report exposure to chemical and biological weapons compared to Veterans without either combat exposure or combat stress (Stuart et al., 2008).

The biological effects of DU were determined in various animal models. Chronic (9 months) ingestion of DU (40 mg/liter) by rats resulted in reduced red blood cell counts that could be explained by the measured effect on kidney function although changes in the spleen could also contribute to this effect (Berradi et al., 2008). Another study of rats chronically (9 months) exposed to either DU or enriched uranium showed that the elevated radioactivity of enriched uranium and not the uranium of DU was more likely responsible for the reduced blood testosterone concentration and the reduced mRNA levels of several genes associated with testicular testosterone synthesis (Grignard et al., 2008).

Nerve Agents

Rodents were used in several studies looking at the effects of nerve agents. Rats with multiple exposures to sarin vapors showed a miotic (i.e., constriction of the pupil of the eye) response although they did not show any measured effects on the heart suggesting that under these experimental conditions the autonomic control in the heart was not affected by sarin (Dabisch et al., 2007). Rats that survived an exposure to a concentration of sarin that resulted in 35 percent mortality after 24 hrs showed a long-lasting reduction in brain function (Grauer et al., 2008). Mice exposed to low dose subcutaneous sarin showed depressed motor activity although concomitant stress with sarin exposure had no additional effect on motor activity; however, the combination of stress and sarin produced delayed behavioral changes and endocrine changes (Mach et al., 2008).

Other vertebrates were also studied. African green monkeys were used to test the sarin concentration needed to cause miosis. The results support the observation that miosis is a valid indicator of exposure to sarin vapor (Genovese et al., 2008). Guinea pigs exposed to repeated sub-lethal doses of the organophosphorus nerve agent soman did not show any changes on a spatial memory test although there was a change in the hippocampal glutamate receptor subunit expression (Johnson et al., 2008). Exposure of guinea pigs to the organophosphorus nerve agents sarin, soman, cyclosarin and tabun resulted in their blood albumin becoming covalently phosphorylated. Consequently, it is possible that the phosphorylated albumin can be used as a marker to determine exposure to these nerve agents (Williams et al., 2007).

Insecticides and Pesticides

The organophosphate insecticide chlorpyrifos, which is a cholinesterase inhibitor, was given to 7-15 day old chickens at various doses. At high doses there were signs of toxicity and of significant inhibition of cholinesterase activity in blood, brain and liver; however, at lower doses repeated over 7 days there were behavior changes but no overt signs of toxicity. These results potentially support the use of 7-15 day old chickens as a model to study the subtle effects of organophosphates on behavior (Al-Badrany and Mohammad, 2007). Transgenic mice lacking P450-paraoxonase 1

(PON1) but expressing human variants of PON1 demonstrated that sensitivity to diazinon is primarily determined by plasma level of PON1 whereas PON1 level and a specific variant of PON1 were more efficient at inactivating chlorpyrifos. Rats chronically exposed to low concentrations of the organophosphate insecticide dichlorvos showed increased Ca2+-uptake by isolated brain mitochondria, decreased brain mitochondrial electron transfer activities and increased brain DNA fragmentation, which suggest enhanced apoptotic neuronal degeneration (Kaur et al., 2007). Rats chronically exposed to dichlorvos for 8 weeks showed reduced body weight gain, reduced brain choline acetyltransferase activity, elevated brain acetylcholinesterase activity, decreased brain muscarinic receptor activity and decrease brain cAMP levels (Raheja and Gill, 2007). Rats sub-chronically intoxicated by chlorfenvinphos, an organophosphate pesticide, had elevated brain activities of several enzymes involved in removing oxidants and had reduced brain glutathione content (Lukaszewicz-Hussain, 2008). Mice with low-dose, long-term exposure to permethrin showed no measured signs of neurotoxicity in striatal dopaminergic neural terminals (Kou and Bloomquist, 2007).

Use of data from a number of primary scientific studies suggested an epidemiological-based link between exposure to acetylcholinesterase inhibitors (i.e. pyridostigmine bromide, pesticides and nerve agents), genotype of enzymes that detoxify acetylcholinesterase inhibitors, activities of detoxifying enzymes and excess health problems in GW Veterans (Golomb, 2008). Human erythrocytes, lymphocytes and brain contain lysophosphatidylcholines hydrolases that show similar sensitivity to inhibition by organophosphate neurotoxicants suggesting that blood cells may provide a means to predict organophosphorus induced neuropathy (Vose et al., 2007).

Jet Fuels

Cell viability and inflammatory response of isolated human epidermal keratinocytes were more sensitive to jet propellant JP-8 than to synthetic S-8 jet fuel (Inman et al., 2008). Synthetic jet fuel (S-8) applied to the skin of mice did not induce immune suppression; however, adding various aromatic hydrocarbon components of military jet fuel (JP-8) to S-8 does lead to immune suppression (Ramos et al., 2007).

C. Immune Dysfunction and Infectious Diseases

(No publications in FY 2008)

D. Reproductive Health

Abu-Musa and co-workers reviewed twenty articles in the existing literature on the effect of conditions of war on female and male reproductive health. For female reproductive health, studies indicated that women who were prisoners of war or who were living in areas exposed to bombardment had increased risk of menstrual abnormalities. Studies of male U.S. and Danish GW Veterans showed no evidence of reduced fertility, but studies of U.K. and Australian Veterans reported increased risk of infertility. Exposure to depleted uranium was not found to have an effect on semen characteristics. The authors stated that most of the studies they examined had major limitations including recall bias and small number of cases included (Abu-Musa et al., 2008).

Feugier and colleagues examined the impact of DU on female gamete quality. They evaluated the effects of DU in drinking water on mouse ovulation and oocytes. DU did not influence ovulation but did affect oocyte quality. The proportion of morphologically healthy oocytes in the exposed group was reduced by half as compared with the control group. The researchers state that more investigations are needed to correlate morphologic assessment of the female gamete with its developmental competence (Feugier et al., 2008).

Verret and co-workers described the outcome and health of the children of French GW Veterans. Data were collected using a self-administered questionnaire completed by 5,666 Gulf Veterans. No specific GW exposure was associated with any birth defect in children fathered after the GW mission. Birth defect incidence in GW children conceived after the mission was similar to birth defect incidence described by the Paris Registry of Congenital Malformations. The authors concluded that the study did not show a high frequency of fertility disorders or miscarriage among French GW Veterans, and there was no link found between paternal exposure during the 1990-1991 Gulf War and increased risk of birth defects among French GW children (Verret et al., 2008).

E. Symptoms and General Health

Chronic fatigue syndrome (CFS), multiple chemical sensitivity (MCS), and fibromyalgia (FM) commonly co-occur. Some propose that CFS, MCS, and FM are manifestations of the same illness based on high rates of co-occurrence and overlapping diagnostic criteria. Although the exact role of the hypothalamo-pituitary-adrenal (HPA) axis in stress-

related disorders such as CFS, FM, chronic pelvic pain, and PTSD is not clear, these conditions are often characterized by alterations in HPA axis activity. There may be some overlap in patient populations in the reports presented below.

General Health

A subset of GW Veterans still on active duty between 1994 and 2004 showed no significant associations between long-term hospitalization and war-related exposures or experiences, with the exception of in-theater hospitalization (Hooper et al., 2008) . There were no measured adverse health effects of vaccinations seen in Australian GW Veterans (Murphy et al., 2007). Comparison of self-reported and recorded vaccinations in Australian GW Veterans found that vaccinations were not associated with adverse health effects when exposure assessment was based on recorded vaccinations (Hooper et al., 2008; Kelsall et al., 2008). Analysis of available epidemiological evidence on cancer risk among GW and Balkans Veterans showed (Lagorio et al., 2008) that the overall incidence of cancers is not increased to date, nor is there consistent evidence of excess risks of neoplasms related to exposure to depleted uranium. Military personnel do display a healthy soldier effect that decreases their risk of mortality compared to the general population (McLaughlin et al., 2008). The overall healthy soldier effect estimate ranges from 10-25 percent, depending on the cause of death studied and the period of follow-up. There is substantial agreement (Smith et al., 2007a) between self-reported and objective deployment information and no clinically meaningful differences in functional health for the small proportion with inconsistent deployment information.

Relying on questionnaire data from a large, random sample of UK GW Veterans, collected in 1996 and 1997, the authors (Cohn et al., 2008) concluded that the nature of GWVI (sometimes referred to as GW Syndrome) as a topic of contestation in the time after the conflict was shaped by rumors, which created a link between specific ideas of the illness with feelings of betrayal, distrust and ambiguity. A second study examined the way in which ill GW Veterans understand their illness to be physical in nature and how they negotiate and resist psychological theories of their illness (Kilshaw, 2008). Veterans in the GW Registry were interviewed in 1995 and 2002 about their medical symptoms and their exposure to war-related hazards and stressors (Brewer et al., 2008). Health symptom reports were strongly correlated between the two time-periods and were stable while recall of war-related exposures was notably unstable. These findings may contribute to understanding some variability in symptoms and exposure recall over time but they do not contribute to understanding GW Veterans' elevated number of unexplained medical symptoms. Using a variety of measurements (i.e., mental, physical and functional health outcomes), a stratified sample of community-residing GW Veterans showed that perceived threat or fear of bodily harm in the war zone and self-reported or perceived exposures to environmental hazards may play a critical role in all measured aspects of health (King et al., 2008). Considerable overlap in symptoms and disease conditions has been noted (Schur et al., 2007b) among medically unexplained and psychiatric conditions such as CFS, low back pain, irritable bowel syndrome, chronic tension headache, FM, temporomandibular joint disorder, major depression, panic attacks, and PTSD. Comorbidity among these nine conditions far exceeded chance expectations, which support theories suggesting that medically unexplained conditions share a common etiology. A study of physicians (Swoboda, 2008) showed that they employ rational decision making for diagnosing controversial illnesses (e.g., CFS, MCS, and GWI) and thereby provide a system of how illnesses lacking conclusive pathogenic and etiological explanations can be diagnosed. Furthermore, the results suggest that diagnosing physicians advance the legitimacy of controversial illnesses by constructing the means for their diagnosis. A histomorphometric analysis of synovial biopsies from individuals with GWVI and joint pain showed that they were no different from synovium from normal individuals and contained similar low-grade inflammatory cell populations consisting almost entirely of macrophages and T-cells (Pessler et al., 2008).

Chronic Pain

Ten active duty US military personnel with newly diagnosed complex regional pain syndrome underwent early intervention with spinal cord stimulation with favorable results, including reduced pain and reduced opioid intake (Verdolin et al., 2007).

Fibromyalgia (FM)

A systematic review (Busch et al., 2008) of studies on the effects of exercise on FM concluded that aerobic-only training has beneficial effects on physical function and some FM symptoms while the effects of strength-only training were less certain but may also improve FM. The underlying mechanism of the neurophysiology in chronic pain seen in FM may involve altered endogenous opioid analgesic activity (Harris et al., 2007). This suggests a possible mechanism for the reduced efficacy of exogenous opiates in those with FM. Electron micrographs of the skin of patients with FM showed unusual patterns of unmyelinated nerve fibers as well as associated Schwann cells (Kim et al., 2008). This suggests that these abnormalities may contribute to or be due to the lower pain threshold seen in patients with FM.

Preliminary evidence (Reiter et al., 2007) suggests that melatonin therapy may be effective in treating FM. After studying various pharmacological and non-pharmacological treatments of fibromyalgia, it was concluded that an individually tailored multidisciplinary pharmacologic, rehabilitative and cognitive-behavioral approach seems to be the most effective (Sarzi-Puttini et al., 2008). A randomized, double blind, placebo-controlled trial showed that nabilone, a synthetic cannabinoid, improved symptoms of FM and was well-tolerated (Skrabek et al., 2008). Unilateral repetitive transcranial magnetic stimulation of the motor cortex induces long-lasting decrease in chronic widespread pain and may constitute an effective alternative analgesic treatment for FM (Passard et al., 2007).

Chronic Fatigue Syndrome (CFS)

The presence of increased heart rate and reduced heart rate variability in patients with CFS during sleep coupled with higher norepinephrine levels and lower plasma aldosterone suggest a state of sympathetic autonomic nervous system predominance and neuroendocrine alterations (Boneva et al., 2007). Two studies demonstrated enhanced glucocorticoid negative feedback and/or a reduced central hypothalamic-pituitary-adrenal (HPA) axis drive in CFS patients (Van Den Eede et al., 2007; Van Den Eede et al., 2008). Most CFS patients have persistent or intermittent gastrointestinal symptoms and those with chronic abdominal complaints showed enterovirus viral capsid protein 1, RNA and non-cytopathic viruses in stomach biopsy specimens (Chia and Chia, 2008). This suggests that a significant subset of CFS patients may have a chronic, disseminated, non-cytolytic form of enteroviral infection that could be diagnosed by stomach biopsy. A comparison of male GW Veterans to male civilians showed that CFS was more likely to present in a sudden flu-like manner in civilians than in Veterans and comorbid fibromyalgia was more prevalent in civilians. A study of fatigue (prolonged fatigue, chronic fatigue and CFS) in twins (Schur et al., 2007a) showed that about half of the variance for both prolonged and chronic fatigue in males was due to genetic effects and half due to individual-specific environmental effects. For females, most variance was due to individual environmental effects. A study comparing GW Veterans and civilians with CFS questioned whether CFS was actually a single clinical entity due to observed differences (Ciccone et al., 2008). An examination of 328 CFS patients' sera examined by a membrane immunobead assay using purified monoclonal anti-ciguatoxin antibody found 91.2 percent gave a titer of 1:40; all 8 GW Veterans' sera samples examined also had a titer of1:40. Over 90 percent of 52 normal sera showed titers of 1:20 or less (Hokama et al., 2008).

F. Abstracts from Published Research

Abu-Musa AA, Kobeissi L, Hannoun AB, Inhorn MC (2008) Effect of war on fertility: a review of the literature. Reprod Biomed Online 17 Suppl 1:43-53.
The aim of this study was to review the existing literature on the effect of war on female and male fertility. A MEDLINE search for studies that included participants defined as infertile because they were unsuccessful in achieving a pregnancy after a year and studies that assessed the effect of war on semen parameters and menstrual dysfunction were performed. Twenty articles were included in this review. For female fertility, studies showed that women who were prisoners of war or who were living in areas exposed to bombardment had increased risk of menstrual abnormalities. For male fertility, the results were conflicting. The Vietnam War was not associated with difficulty in conception although one study revealed a decrease in sperm characteristics. Studies of male US and Danish 1990/91 GW veterans showed no evidence of reduced fertility; however, studies of UK and Australian veterans reported increased risk of infertility. The Lebanese and Slovenian civil wars were associated with a decrease in sperm parameters. Exposure to mustard gas was also associated with abnormal semen parameters; however, exposure to depleted uranium had no effect on semen characteristics. Most of the studies examined had major limitations including recall bias and small number of cases included.

Al-Badrany YM, Mohammad FK (2007) Effects of acute and repeated oral exposure to the organophosphate insecticide chlorpyrifos on open-field activity in chicks. Toxicol Lett 174:110-116.
The effects of the organophosphate insecticide chlorpyrifos on 5min open-field activity were examined in a 7-15 days old chick model. Chlorpyrifos was acutely administered taking into account cholinesterase inhibition and determination of the acute (24h) median lethal dose (LD_{50}). The oral LD_{50} value of chlorpyrifos in chicks was 18.14mg/kg, with cholinergic toxicosis observed on intoxicated chicks. Chlorpyrifos at the dose rates of 5, 10 and 20mg/kg orally produced within 2h signs of cholinergic toxicosis in the chicks and significantly inhibited plasma (40-70%), whole brain (43-69%) and liver (31-46%) cholinesterase activities in a dose-dependent manner. Chlorpyrifos at 2 and 4mg/kg, orally did not produce overt signs of cholinergic toxicosis, but decreased (30, 60 and 90min after dosing) the general locomotor activity of the chicks as seen by a significant increase in the latency to move from the central square of the open-field arena, decreases in the numbers of lines crossed and vocalization score. Repeated daily chlorpyrifos treatments (2 and 4mg/kg, orally) for seven consecutive days also caused hypoactivity in chicks in the open-field

behavioral paradigm. Only the high dose of chlorpyrifos (4mg/kg, orally) given repeatedly for 7 days caused significant cholinesterase inhibition in the whole brain (37%) and the liver (22%). In conclusion, chlorpyrifos at single or short-term repeated doses-induced behavioral changes in 7-15 days old chicks, in a model that could be used for further neurobehavioral studies involving subtle effects of organophosphates on chicks.

Allen KD, Kasarskis EJ, Bedlack RS, Rozear MP, Morgenlander JC, Sabet A, Sams L, Lindquist JH, Harrelson ML, Coffman CJ, Oddone EZ (2008) The National Registry of Veterans with amyotrophic lateral sclerosis. Neuroepidemiology 30:180-190.
BACKGROUND: The Department of Veterans Affairs (VA) Cooperative Studies Program has established a National Registry of Veterans with Amyotrophic Lateral Sclerosis (ALS). This article describes the objectives, methods, and sample involved in the registry. METHODS: United States military veterans with ALS were identified through national VA electronic medical record databases and nationwide publicity efforts for an enrollment period of 4 1/2 years. Diagnoses were confirmed by medical record reviews. Registrants were asked to participate in a DNA bank. Follow-up telephone interviews are conducted every 6 months to track participants' health status. RESULTS: As of September 30, 2007, 2,400 veterans had consented to participate in the registry, 2,068 were included after medical record review, 995 were still living and actively participating, and 1,573 consented to participate in the DNA bank. 979 participants had been enrolled in the registry for at least 1 year, 497 for at least 2 years, and 205 for at least 3 years. Fourteen studies have been approved to use registry data for epidemiological, observational, and interventional protocols. CONCLUSION: This registry has proven to be a successful model for identifying large numbers of patients with a relatively rare disease and enrolling them into multiple studies, including genetic protocols.

Al-Turkait FA, Ohaeri JU (2008) Post-traumatic stress disorder among wives of Kuwaiti veterans of the first Gulf War. J Anxiety Disord 22:18-31.
OBJECTIVES: To assess post-traumatic stress disorder (PTSD) among wives of Gulf War Kuwaiti military men, divided into four groups according to degree of combat exposure: the retired, an active-in-the-army group (AIA) (involved in duties at the rear); an in-battle group (IB) (involved in combat); and a prisoners-of-war (POWs) group. To assess the relationship between wives' PTSD and indices of family adjustment, husbands' level of combat exposure, and PTSD status. METHOD: One hundred and seventy-six wives were assessed with the PTSD Checklist for DSM-IV, the family adjustment device, and for anxiety/depression. RESULTS: Fifty (28.4%) fulfilled criteria for probable PTSD. The prevalence was significantly associated with husbands' combat exposure, her presence in Kuwait, but not with husbands' PTSD status. Wives' PTSD was mostly predicted by their depression/anxiety scores. CONCLUSION: The findings support the salience of effective social support, and the need for women empowerment issues in psychosocial intervention for this group.

Al-Turkait FA, Ohaeri JU (2008) Prevalence and correlates of posttraumatic stress disorder among Kuwaiti military men according to level of involvement in the first Gulf War. Depress Anxiety 25:932-941.
First, to compare the prevalence and intensity of posttraumatic stress disorder (PTSD) among Kuwaiti military men, divided into four groups (50 subjects each) according to degree of exposure to war trauma: (1) the retired (retired before the invasion); (2) an active-in-the-army group (AIA) (involved in duties at the rear only); (3) an in-battle (IB) group (involved in combat); and (4) prisoners of war (POWs-captured during combat). Second, to compare the severity of impact of event, comorbid depression, and anxiety among the groups. Third, to evaluate the contribution of self-esteem and locus of control (LOC). Subjects were interviewed once, 6 years after the war, using: the Clinician Administered PTSD Scale; the Impact of Event Scale (IES); the Hopkins Symptom Checklist-25; the Internal-External LOC; and The Self-Esteem Scale. Subjects were aged 24-71 years (mean 37.9). Sixty-three subjects (31.5%) fulfilled criteria for PTSD, with the rate significantly higher among the POWs (48%) than the retired (24%) and IB (22%), reflecting the severity of IES. Avoidance symptoms were the most pronounced. Self-esteem was significantly lowest among the POWs and those with PTSD. External LOC was associated with PTSD, anxiety, and depression. Self-esteem was the only covariate of PTSD scores. LOC was a significant covariate for anxiety. The characteristics of PTSD in these veterans showed similarity with those from elsewhere. The prominence of self-esteem and avoidance symptoms implies that they should be part of focus for interventions. Focus on LOC should be from the perspective of anxiety.

Al-Turkait FA, Ohaeri JU (2008) Psychopathological status, behavior problems, and family adjustment of Kuwaiti children whose fathers were involved in the first gulf war. Child Adolesc Psychiatry Ment Health 2:12.
OBJECTIVES: Following the end of the Gulf War that resulted in the liberation of Kuwait, there are no reports on the impact of veterans' traumatic exposure and posttraumatic stress disorder (PTSD) on their children. We compared the severity of anxiety, depression, deviant behavior and poor family adjustment among the children of a stratified random sample of four groups of Kuwaiti military men, viz: the retired; an active -in-the-army group (AIA) (involved in duties at the rear); an in-battle group (IB) (involved in combat); and a prisoners -of- war (POWs) group. Also, we assessed the

association of father's PTSD/combat status and mother's characteristics with child psychosocial outcomes. METHOD: Subjects were interviewed at home, 6 years after the war, using: the Child Behavior Index to assess anxiety, depression, and adaptive behavior; Rutter Scale A2 for deviant behavior; and Family Adjustment Device for adjustment at home. Both parents were assessed for PTSD. RESULTS: The 489 offspring (250 m, 239 f; mean age 13.8 yrs) belonged to 166 father-mother pairs. Children of POWs tended to have higher anxiety, depression, and abnormal behavior scores. Those whose fathers had PTSD had significantly higher depression scores. However, children of fathers with both PTSD and POW status (N = 43) did not have significantly different outcome scores than the other father PTSD/combat status groups. Mother's PTSD, anxiety, depression and social status were significantly associated with all the child outcome variables. Parental age, child's age and child's level of education were significant covariates. Although children with both parents having PTSD had significantly higher anxiety/depression scores, the mother's anxiety was the most frequent and important predictor of child outcome variables. The frequency of abnormal test scores was: 14% for anxiety/depression, and 17% for deviant behavior. CONCLUSION: Our findings support the impression that child emotional experiences in vulnerable family situations transcend culture and are associated with the particular behavior of significant adults in the child's life. The primacy of the mother's influence has implications for interventions to improve the psychological functioning of children in such families. Mental health education for these families has the potential to help those in difficulty.

Berradi H, Bertho JM, Dudoignon N, Mazur A, Grandcolas L, Baudelin C, Grison S, Voisin P, Gourmelon P, Dublineau I (2008) Renal anemia induced by chronic ingestion of depleted uranium in rats. Toxicol Sci 103:397-408.

Kidney disease is a frequent consequence of heavy metal exposure and renal anemia occurs secondarily to the progression of kidney deterioration into chronic disease. In contrast, little is known about effects on kidney of chronic exposure to low levels of depleted uranium (DU). Study was performed with rats exposed to DU at 40 mg/l by chronic ingestion during 9 months. In the present work, an approximately 20% reduction in red blood cell (RBC) count was observed after DU exposure. Hence, three hypotheses were tested to determinate origin of RBC loss: (1) reduced erythropoiesis, (2) increased RBC degradation, and/or (3) kidney dysfunction. Erythropoiesis was not reduced after exposure to DU as revealed by erythroid progenitors, blood Flt3 ligand and erythropoietin (EPO) blood and kidney levels. Concerning messenger RNA (mRNA) and protein levels of spleen iron recycling markers from RBC degradation (DMT1 [divalent metal transporter 1], iron regulated protein 1, HO1, HO2 [heme oxygenase 1 and 2], cluster of differentiation 36), increase in HO2 and DMT1 mRNA level was induced after chronic exposure to DU. Kidneys of DU-contaminated rats had more frequently high grade tubulo-interstitial and glomerular lesions, accumulated iron more frequently and presented more apoptotic cells. In addition, chronic exposure to DU induced increased gene expression of ceruloplasmin (x12), of DMT1 (x2.5), and decreased mRNA levels of erythropoietin receptor (x0.2). Increased mRNA level of DMT1 was associated to decreased protein level (x0.25). To conclude, a chronic ingestion of DU leads mainly to kidney deterioration that is probably responsible for RBC count decrease in rats. Spleen erythropoiesis and molecules involved in erythrocyte degradation were also modified by chronic DU exposure.

Bland DJ, Rona RJ, Coggon D, Anderson J, Greenberg N, Hull L, Wessely S (2007) Urinary isotopic analysis in the UK Armed Forces: No evidence of depleted uranium absorption in combat and other personnel in Iraq. Occup Environ Med.

OBJECTIVES: To assess the distribution and risk factors of DU uptake in military personnel who had taken part in the invasion of Iraq in 2003. METHODS: Sector field inductively coupled plasma-mass spectrometry (SF-ICP-MS) was used to determine the uranium concentration and $^{238}U/^{235}U$ isotopic ratio in spot urine samples. We collected urine samples from four groups identified a priori as having different potential for exposure to DU. These groups were: combat personnel (n=199); non-combat personnel (n=96); medical personnel (n=22); and "clean-up" personnel (n=24) who had been involved in the maintenance, repair or clearance of potentially contaminated vehicles in Iraq. A short questionnaire was used to ascertain individual experience of circumstances in which DU exposure might have occurred. RESULTS: There was no statistically significant difference in the 238U/235U ratio between groups. Mean ratios by group varied from 138.0 (95% CI 137.3-138.7) for clean-up personnel to 138.2 (95% CI 138.0-138.5) for combat personnel, and were close to the ratio of 137.9 for natural uranium. The two highest individual ratios (146.9 and 147.7) were retested using more accurate, multiple collector inductively coupled plasma-mass spectrometry (MC-ICP-MS) and found to be within measurement of error of that for natural uranium. There were no significant differences in isotope ratio between participants according to self-reported circumstances of potential DU exposure. CONCLUSIONS: Based on measurements using a SF-ICP-MS apparatus, our study provides reassurance following concern for potential widespread DU uptake in the UK military. The rare occurrence of elevated ratios may reflect the limits of accuracy of the SF-ICP-MS apparatus and not a real increase from the natural proportions of the isotopes. Any uptake of DU among

participants in this study sample would be very unlikely to have any implications for health. Keywords: Military, $^{238}U/^{235}U$, Iraq War, Depleted Uranium, SF-ICP-MS.

Boneva RS, Decker MJ, Maloney EM, Lin JM, Jones JF, Helgason HG, Heim CM, Rye DB, Reeves WC (2007) Higher heart rate and reduced heart rate variability persist during sleep in chronic fatigue syndrome: a population-based study. Auton Neurosci 137:94-101.
Autonomic nervous system (ANS) dysfunction has been suggested in patients with chronic fatigue syndrome (CFS). In this study, we sought to determine whether increased heart rate (HR) and reduced heart rate variability (HRV) parameters observed in CFS patients during wakefulness persist during sleep. To this end, we compared heart rate (HR) and HRV as indicators of ANS function in CFS subjects and non-fatigued (NF) controls in a population-based, case-control study. Thirty subjects with CFS and 38 NF controls, matched for age-, sex- and body mass index, were eligible for analysis. Main outcome measures included mean RR interval (RRI), HR, and HRV parameters derived from overnight ECG. Plasma aldosterone and norepinephrine levels, medicines with cardiovascular effect, and reported physical activity were examined as covariates. General Linear Models were used to assess significance of associations and adjust for potential confounders. Compared to controls, CFS cases had significantly higher mean HR (71.4 vs 64.8 bpm), with a shorter mean RRI [840.4 (85.3) vs 925.4(97.8) ms] ($p<0.0004$, each), and reduced low frequency (LF), very low frequency (VLF), and total power (TP) of HRV ($p<0.02$, all). CFS cases had significantly lower plasma aldosterone ($p<0.05$), and tended to have higher plasma norepinephrine levels. HR correlated weakly with plasma norepinephrine ($r=0.23$, $p=0.05$) and moderately with vitality and fatigue scores ($r=-0.49$ and 0.46, respectively, $p<0.0001$). Limitation in moderate physical activity was strongly associated with increased HR and decreased HRV. Nevertheless, among 42 subjects with similar physical activity limitations, CFS cases still had higher HR (71.8 bpm) than respective controls (64.9 bpm), $p=0.023$, suggesting that reduced physical activity could not fully explain CFS-associated differences in HR and HRV. After adjusting for potential confounders case-control differences in HR and TP remained significant ($p<0.05$). Conclusion: the presence of increased HR and reduced HRV in CFS during sleep coupled with higher norepinephrine levels and lower plasma aldosterone suggest a state of sympathetic ANS predominance and neuroendocrine alterations. Future research on the underlying pathophysiologic mechanisms of the association is needed.

Brewer NT, Hallman WK, Kipen HM (2008) The symmetry rule: a seven-year study of symptoms and explanatory labels among Gulf War veterans. Risk Anal 28:1737-1748.
Noticing medical symptoms can cause one to search for explanatory labels such as "ate bad food" or even "exposed to anthrax," and perhaps these labels may cause new symptom reports. The present study examined whether there is empirical support for this symptom-label "symmetry rule." We interviewed veterans (N= 362) from the Gulf War Registry in 1995 and 2002 about their medical symptoms and about their exposure to war-related hazards and stressors. Health symptom reports were strongly correlated between the two time periods and showed relatively stable mean levels, whereas recall of war-related exposures was notably unstable. Veterans starting with fewer medical symptoms recalled fewer war-related exposures seven years later. Initial recollection of chemical and biological warfare exposure (but not other exposures) longitudinally predicted novel medical symptoms. The findings generally support the symmetry rule hypotheses, although the evidence for the label to symptom link was less strong. The findings account for some variability in symptoms and exposure recall over time, but they do not, on their own, account for the Gulf War Veterans' elevated number of unexplained medical symptoms.

Busch AJ, Schachter CL, Overend TJ, Peloso PM, Barber KA (2008) Exercise for fibromyalgia: a systematic review. J Rheumatol 35:1130-1144.
OBJECTIVE: Fibromyalgia (FM) is a syndrome expressed by chronic widespread pain often associated with reduced physical function. Exercise is a common recommendation in management of FM. We evaluated the effects of exercise training on global well-being, selected signs and symptoms, and physical function in individuals with FM. METHODS: We searched Medline, Embase, CINAHL, SportDiscus, PubMed, PEDro, and the Cochrane Central Register for Controlled Trials to July 2005 and included randomized trials evaluating cardiorespiratory endurance, muscle strength, and flexibility. Methodological quality was assessed using the van Tulder and Jadad instruments. Training protocols were evaluated using American College of Sports Medicine (ACSM) guidelines. Clinical heterogeneity limited metaanalysis to 6 aerobic and 2 strength studies. RESULTS: There were 2276 subjects across the 34 studies; 1264 subjects were assigned to exercise interventions. Metaanalysis of 6 studies provided moderate-quality evidence that aerobic-only exercise training at ACSM-recommended intensity levels has positive effects on global well-being (SMD 0.49, 95% CI 0.23-0.75) and physical function (SMD 0.66, 95% CI 0.41-0.92) and possibly on pain (SMD 0.65, 95% CI -0.09 to 1.39) and tender points (SMD 0.23, 95% CI -0.18 to 0.65). Strength and flexibility remain underevaluated; however, strength training may have a positive effect on FM symptoms. CONCLUSION: Aerobic-only training has

beneficial effects on physical function and some FM symptoms. Strength-only training may improve FM symptoms, but requires further study. Large, high-quality studies of exercise-only interventions that provide detailed information on exercise prescription and adherence are needed.

Cazoulat A, Lecompte Y, Bohand S, Castagnet X, Laroche P (2008) [Urinary uranium analysis results on Gulf war or Balkans conflict veterans]. Pathol Biol (Paris) 56:77-83.
During the 1991 Gulf War, the 1995 Bosnia conflict and the 1999 Kosovo conflict, munitions containing depleted uranium (DU) have been employed by the coalition forces. Although the radioactivity of this metal is about 40-50% lower than that of natural uranium, and that health concerns are based primarily on the metal's kidney toxicity, DU has been quoted among the causes of the different pathologies developed by some soldiers a few time after they went back home. In order to evaluate the potential relation between a DU exposition and some of the pathologies described, more than 200 urine uranium analysises have been done between 1999 and 2003 by the laboratory of the french Army radioprotection service. The method used is the standard method for determining uranium in excretion of nuclear workers: a chemical uranium isotopes separation (including 234, 235+236 and 238) followed by an alpha ray spectrometry. All results were negative and quite all of the detection limits were lower than the ones recommended by the International Commission on Radiological Protection (10mBq/L per isotope). The summary is that none of the available analysises for uranium excreted in urine suggests that any subjects examined had incorporated DU that could explain pathologies appeared after the conflicts.

Chia JK, Chia AY (2008) Chronic fatigue syndrome is associated with chronic enterovirus infection of the stomach. J Clin Pathol 61:43-48.
BACKGROUND AND AIMS: The aetiology for chronic fatigue syndrome (CFS) remains elusive although enteroviruses have been implicated as one of the causes by a number of studies. Since most CFS patients have persistent or intermittent gastrointestinal (GI) symptoms, the presence of viral capsid protein 1 (VP1), enterovirus (EV) RNA and culturable virus in the stomach biopsy specimens of patients with CFS was evaluated. METHODS: 165 consecutive patients with CFS underwent upper GI endoscopies and antrum biopsies. Immunoperoxidase staining was performed using EV-specific monoclonal antibody (mAb) or a control mAb specific for cytomegalovirus (CMV). RT-PCR ELISA was performed on RNA extracted from paraffin sections or samples preserved in RNA later. Biopsies from normal stomach and other gastric diseases served as controls. 75 samples were cultured for EV. RESULTS: 135/165 (82%) biopsies stained positive for VP1 within parietal cells, whereas 7/34 (20%) of the controls stained positive ($p< or =0.001$). CMV mAb failed to stain any of the biopsy specimens. Biopsies taken from six patients at the onset of the CFS/abdominal symptoms, and 2-8 years later showed positive staining in the paired specimens. EV RNA was detected in 9/24 (37%) paraffin-embedded biopsy samples; 1/21 controls had detectable EV RNA ($p<0.01$); 1/3 patients had detectable EV RNA from two samples taken 4 years apart; 5 patient samples showed transient growth of non-cytopathic enteroviruses. CONCLUSION: Enterovirus VP1, RNA and non-cytopathic viruses were detected in the stomach biopsy specimens of CFS patients with chronic abdominal complaints. A significant subset of CFS patients may have a chronic, disseminated, non-cytolytic form of enteroviral infection, which could be diagnosed by stomach biopsy.

Ciccone DS, Weissman L, Natelson BH (2008) Chronic fatigue syndrome in male Gulf war veterans and civilians: a further test of the single syndrome hypothesis. J Health Psychol 13:529-536.
Abstract: Different modes of fatigue onset in male Gulf War Veterans versus male civilians raise the possibility that chronic fatigue syndrome (CFS) may not be a single disease entity. We addressed this issue by comparing 45 male veterans with CFS to 84 male civilians who satisfied identical case criteria. All were evaluated for fibromyalgia (FM), multiple chemical sensitivity and psychiatric comorbidity. CFS was more likely to present in a sudden flu-like manner in civilians than veterans ($p < .01$) and comorbid FM was more prevalent in civilians ($p < .01$). These findings question the assumption that all patients with CFS suffer from the same underlying disorder.

Cohn S, Dyson C, Wessely S (2008) Early accounts of Gulf War illness and the construction of narratives in UK service personnel. Soc Sci Med 67:1641-1649.
"Gulf War Syndrome" has become firmly established in public and political discourse, and considerable numbers of veterans of the 1991 Gulf war now see it as part of their identity. In this paper we draw on open-ended questionnaire data drawn from a large, random sample of UK Gulf veterans, collected in 1996 and 1997. Whilst there is already some literature focusing on coherent personal narratives of some veterans and campaigners, we suggest that they are preceded by much more fragmentary, shared accounts. We take the idea of rumour as a way of encapsulating how these partial ideas swiftly gained value by reflecting and reproducing social ties. Accounts describing fears about this mystery condition simultaneously made reference to concerns about their role as a soldier, about the purpose of the conflict, and rising mistrust of their commanders. As doubt over soldiers' function increased, informal social networks became increasingly significant, perhaps also linked to an erosion of respect for formal military hierarchy. At the same time,

rumours of "Gulf War Syndrome" began to circulate, reinforcing the idea that the cause was elusive, and invisible, whilst undermining both the unity of the military force and the individual soldier's body. We suggest that the nature of Gulf War Syndrome as a topic of contestation in the years after the conflict was keenly shaped by these early rumours, which entangled specific ideas of the illness with feelings of betrayal, distrust and ambiguity. Informed by the general literature on illness narratives, we explore how the transmission of ideas and causal theories were themselves instrumental in the emergence of the condition as it was experienced.

Dabisch PA, To F, Kerut EK, Horsmon MS, Mioduszewski RJ (2007) Multiple exposures to sarin vapor result in parasympathetic dysfunction in the eye but not the heart. Toxicol Sci 99:354-361.
Several studies in conscious animals have reported parasympathetic dysfunction in the eyes following exposure to cholinesterase inhibitors. Given the similarities between the autonomic innervation in the eye and the heart, it is possible that parasympathetic dysfunction could also occur in the heart. Therefore, the present study assessed time domain indices of heart rate variability in conscious rats surgically implanted with telemetric transmitters to investigate the hypothesis that multiple exposures to the nerve agent sarin would result in muscarinic receptor desensitization and parasympathetic dysfunction in the heart. Animals exposed to sarin vapor on multiple occasions developed parasympathetic dysfunction in the eye characterized by an attenuated response to light and a diminished miotic response to sarin vapor exposure. However, the same dose of sarin vapor failed to produce any effects on either time domain indices of HRV or the magnitude of the tachycardia induced by atropine, suggesting that autonomic control in the heart was not affected. It is possible that the dose of sarin used in the present study was insufficient to inhibit cardiac acetylcholinesterase (AChE). Additional studies utilizing higher doses of sarin may be able to inhibit cardiac AChE, producing overstimulation of cardiac muscarinic receptors, ultimately resulting in desensitization and parasympathetic dysfunction.

Feugier A, Frelon S, Gourmelon P, Claraz M (2008) Alteration of mouse oocyte quality after a subchronic exposure to depleted Uranium. Reprod Toxicol 26:273-277.
Gametes and embryo tissues are known to represent a sensitive target to environmental toxicants exposure. Oocyte quality can impact subsequent developmental competence, pregnancy course and even adult health. The major health concern from depleted uranium (DU) is mainly centred on its chemotoxic properties as a heavy metal. Little attention was paid to the impact of uranium on female gamete quality. The aim of this research was to evaluate the effect of DU on mouse oocyte quality after 49 days of subchronic contamination in drinking water and to correlate the observed effects with the amount of DU accumulated in organs. Four different DU concentrations were investigated: 0 (control), 10 (DU10), 20 (DU20) and 40 mg/L (DU40). DU did not influence the intensity of ovulation but affected oocyte quality. The proportion of healthy oocytes was reduced by half ($P<0.001$) from 20 mg/L compared with control group (0.537; 0.497; 0.282 and 0.239 in control, DU10, DU20 and DU40 groups respectively) whereas no accumulation of DU was recorded in the ovaries whatever the dose tested. Abnormal perivitelline space ($P<0.001$) or absence of the 1st polar body ($P<0.001$) was identified as the main characteristic of DU impact. In the context of this study, the NOAEL for oocyte quality was determined at 10 mg/L in drinking water (1.9 mg /kg/day). An increase in the dose of contamination over 20 mg/L did not amplify the proportion of oocytes contracting a specific alteration but conducted to a diversification in oocytes abnormalities. Further investigations are necessary to correlate morphologic assessment of female gamete with its developmental competence.

Fontana A, Rosenheck R (2008) Treatment-seeking veterans of Iraq and Afghanistan: comparison with veterans of previous wars. J Nerv Ment Dis 196:513-521.
Differences in the characteristics and mental health needs of veterans of the Iraq/Afghanistan war when compared with those of veterans who served in the Persian Gulf war and in the Vietnam war may have important implications for Veterans Affairs (VA) program and treatment planning. Subjects were drawn from administrative data bases of veterans who sought treatment from specialized VA programs for treatment of posttraumatic stress disorder (PTSD). Current Iraq/Afghanistan veterans were compared with 4 samples of outpatient and inpatient Persian Gulf and Vietnam veterans whose admission to treatment was either contemporaneous or noncontemporaneous with their admission. A series of analyses of covariance was used hierachically to control for program site and age. In analyses of contemporaneous veterans uncontrolled for age, Iraq/Afghanistan veterans differed most notably from Vietnam veterans by being younger, more likely to be female, less likely to be either married or separated/divorced, more often working, less likely to have ever been incarcerated, and less likely to report exposure to atrocities in the military. Regarding clinical status, Iraq/Afghanistan veterans were less often diagnosed with substance abuse disorders, manifested more violent behavior, and had lower rates of VA disability compensation because of PTSD. Differences are more muted in comparisons with Persian Gulf veterans, particularly in those involving noncontemporaneous samples, or those that controlled for age differences. Among recent war veterans with PTSD, social functioning has largely been left intact. There is a window of

opportunity, therefore, for developing and focusing on treatment interventions that emphasize the preservation of these social assets.

Genovese RF, Benton BJ, Oubre JL, Fleming PJ, Jakubowski EM, Mioduszewski RJ (2008) Determination of miosis threshold from whole-body vapor exposure to sarin in African green monkeys. Toxicology 244:123-132.
We determined the threshold concentration of sarin vapor exposure producing miosis in African green monkeys (Chlorocebus aethiops). Monkeys (n=8) were exposed to a single concentration of sarin (0.069-0.701mg/m^3) for 10min. Changes in pupil size were measured from photographs taken before and after the exposure. Sarin EC_{50} values for miosis were determined to be 0.166mg/m^3 when miosis was defined as a 50% reduction in pupil area and 0.469mg/m^3 when miosis was defined as a 50% reduction in pupil diameter. Monkeys were also evaluated for behavioral changes from sarin exposure using a serial probe recognition test and performance remained essentially unchanged for all monkeys. None of the concentrations of sarin produced specific clinical signs of toxicity other than miosis. Sarin was regenerated from blood sampled following exposure in a concentration-dependent fashion. Consistent with a predominant inhibition of acetylcholinesterase (AChE), more sarin was consistently found in RBC fractions than in plasma fractions. Further, elimination of regenerated sarin from RBC fractions was slower than from plasma fractions. Blood samples following exposure also showed concentration-dependent inhibition of AChE activity and, to a lesser extent, butyrylcholinesterase activity. At the largest exposure concentration, AChE inhibition was substantial, reducing activity to approximately 40% of baseline. The results characterize sarin exposure concentrations that produce miosis in a large primate species in the absence of other overt signs of toxicity. Further, these results extend previous studies indicating that miosis is a valid early indicator for the detection of sarin vapor exposure.

Golomb BA (2008) Acetylcholinesterase inhibitors and Gulf War illnesses. Proc Natl Acad Sci U S A 105:4295-4300.
Increasing evidence suggests excess illness in Persian Gulf War Veterans (GWV) can be explained in part by exposure of GWV to organophosphate and carbamate acetylcholinesterase inhibitors (AChEis), including pyridostigmine bromide (PB), pesticides, and nerve agents. Evidence germane to the relation of AChEis to illness in GWV was assessed. Many epidemiological studies reported a link between AChEi exposure and chronic symptoms in GWV. The link is buttressed by a dose-response relation of PB pill number to chronic symptoms in GWV and by a relation between avidity of AChEi clearance and illness, based on genotypes, concentrations, and activity levels of enzymes that detoxify AChEis. Triangulating evidence derives from studies linking occupational exposure to AChEis to chronic health symptoms that mirror those of ill GWV. Illness is again linked to lower activity of AChEi detoxifying enzymes and genotypes conferring less-avid AChEi detoxification. AChEi exposure satisfies Hill's presumptive criteria for causality, suggesting this exposure may be causally linked to excess health problems in GWV.

Grauer E, Chapman S, Rabinovitz I, Raveh L, Weissman BA, Kadar T, Allon N (2008) Single whole-body exposure to sarin vapor in rats: long-term neuronal and behavioral deficits. Toxicol Appl Pharmacol 227:265-274.
Freely moving rats were exposed to sarin vapor (34.2±0.8 μg/l) for 10 min. Mortality at 24 h was 35% and toxic sings in the surviving rats ranged from sever (prolonged convulsions) through moderate to almost no overt signs. Some of the surviving rats developed delayed, intermittent convulsions. All rats were evaluated for long-term functional deficits in comparison to air-exposed control rats. Histological analysis revealed typical cell loss at 1 week post inhalation exposure. Neuronal inflammation was demonstrated by a 20-fold increase in prostaglandin (PGE_2) levels 24 h following exposure that markedly decreased 6 days later. An additional, delayed increase in PGE_2 was detected at 1 month and continued to increase for up to 6 months post exposure. Glial activation following neural damage was demonstrated by an elevated level of peripheral benzodiazepine receptors (PBR) seen in the brain 4 and 6 months after exposure. At the same time muscarinic receptors were unaffected. Six weeks, four and six months post exposure behavioral evaluations were performed. In the open field, sarin-exposed rats showed a significant increase in overall activity with no habituation over days. In a working memory paradigm in the water maze, these same rats showed impaired working and reference memory processes with no recovery. Our data suggest long lasting impairment of brain functions in surviving rats following a single sarin exposure. Animals that seem to fully recover from the exposure, and even animals that initially show no toxicity signs, developed some adverse neural changes with time.

Grignard E, Gueguen Y, Grison S, Lobaccaro JM, Gourmelon P, Souidi M (2008) Contamination with depleted or enriched uranium differently affects steroidogenesis metabolism in rat. Int J Toxicol 27:323-328.
Uranium is a naturally occurring heavy metal found in the Earth's crust. It is an alpha-emitter radioactive element from the actinide group that presents both radiotoxicant and chemotoxicant properties. Some studies revealed that uranium could affect the reproductive system. To distinguish chemical versus radiological effects of uranium on the metabolism of the steroids in the testis, rats were contaminated via their drinking water with depleted or enriched uranium. Animals

were exposed to radionuclides for 9 months at a dose of 40 mg/L (560 Bq/L for depleted uranium, 1680 Bq/L for enriched uranium). Whereas depleted uranium did not seem to significantly affect the production of testicular steroid hormones in rats, enriched uranium significantly increased the level of circulating testosterone by 2.5-fold. Enriched uranium contamination led to significant increases in the mRNA levels of StAR (Steroidogenic Acute Regulatory protein; 3-fold, p = .001), cyp11a1 (cytochrome P45011a1; 2.2-fold, p < .001), cyp17a1 (cytochrome P45017a1; 2.5-fold, p = .014), cyp19a1 (cytochrome P45019a1; 2.3-fold, p = .021), and 5α R1 (5α reductase type 1; 2.0-fold, p = .02), whereas depleted uranium contamination induces no changes in the expression of these genes. Moreover, expression levels of the nuclear receptors LXR (Liver X Receptor) and SF-1 (Steroidogenic Factor 1), as well as the transcription factor GATA-4, were modified following enriched uranium contamination. Altogether, these results show for the first time a differential effect among depleted or enriched uranium contamination on testicular steroidogenesis. It appears that the deleterious effects of uranium are mainly due to the radiological activity of the compound.

Harris RE, Clauw DJ, Scott DJ, McLean SA, Gracely RH, Zubieta JK (2007) Decreased central mu-opioid receptor availability in fibromyalgia. J Neurosci 27:10000-10006.
The underlying neurophysiology of acute pain is fairly well characterized, whereas the central mechanisms operative in chronic pain states are less well understood. Fibromyalgia (FM), a common chronic pain condition characterized by widespread pain, is thought to originate largely from altered central neurotransmission. We compare a sample of 17 FM patients and 17 age- and sex-matched healthy controls, using mu-opioid receptor (MOR) positron emission tomography. We demonstrate that FM patients display reduced MOR binding potential (BP) within several regions known to play a role in pain modulation, including the nucleus accumbens, the amygdala, and the dorsal cingulate. MOR BP in the accumbens of FM patients was negatively correlated with affective pain ratings. Moreover, MOR BP throughout the cingulate and the striatum was also negatively correlated with the relative amount of affective pain (McGill, affective score/sensory score) within these patients. These findings indicate altered endogenous opioid analgesic activity in FM and suggest a possible reason for why exogenous opiates appear to have reduced efficacy in this population.

Hokama Y, Empey-Campora C, Hara C, Higa N, Siu N, Lau R, Kuribayashi T, Yabusaki K (2008) Acute phase phospholipids related to the cardiolipin of mitochondria in the sera of patients with chronic fatigue syndrome (CFS), chronic Ciguatera fish poisoning (CCFP), and other diseases attributed to chemicals, Gulf War, and marine toxins. J Clin Lab Anal 22:99-105.
This study examined 328 CFS sera in a study with 17 CCFP, 8 Gulf War Veterans (GWV), 24 Prostate Cancer (PC), and 52 normal sera in the modified Membrane Immunobead Assay (MIA) procedure for CTX. Three hundred and twenty-eight CFS patients' sera were examined by the modified MIA with purified MAb-CTX and 91.2% gave a titre > or =1:40. 76% of the 17 CCFP sera samples and 100% of the 8 GWV sera samples also had a titre > or =1:40. 92.3% of 52 normal sera showed titres of 1:20 or less, while 4 gave titres of > or =1:40. In addition, 41 sera were examined for Anti-Cardiolipin (aCL) by a commercial ELISA procedure with 87.8% demonstrating IgM, IgM+IgA, or IgM+IgG aCL antibodies. These results showed mostly the IgM aCL antibody alone in the sera samples. In addition, 41 serum samples were examined for aCL, with 37 showing positive for aCL, representing 90.2% positive for the three disease categories examined: CFS, CCFP and GWV. Examination for antiMitochondrial-M2 autoantibody (aM-M2) in 28 patients (CFS (18), CCFP (5), and GWV (5)) was negative for aM-M2. Inhibition analysis with antigens, CTX, CFS "Acute Phase Lipids", commercial Cardiolipin (CL) and 1,2-Dipalmitoyl-sn-Glycero-3-[Phospho-L-Serine] (PS) and antibodies, MAb-CTX and aCL from patients' serum show that the phospholipids in CL and CTX are antigenically indistinguishable with antibodies MAb-CTX and CFS-aCL. Preliminary chemical analyses have shown the lipids to be phospholipids associated with CL of the mitochondria. We designate this "Acute Phase Lipid" comparable to "Acute Phase Proteins" (C-reactive protein (CRP) and Serum Amyloid A (SAA)) in inflammatory conditions.

Hooper TI, DeBakey SF, Nagaraj BE, Bellis KS, Smith B, Smith TC, Gackstetter GD (2008) The long-term hospitalization experience following military service in the 1991 Gulf War among veterans remaining on active duty, 1994-2004. BMC Public Health 8:60.
BACKGROUND: Despite more than a decade of extensive, international efforts to characterize and understand the increased symptom and illness-reporting among veterans of the 1991 Gulf War, concern over possible long-term health effects related to this deployment continue. The purpose of this study was to describe the long-term hospitalization experience of the subset of U.S. Gulf War Veterans still on active duty between 1994 and 2004. METHODS: Gulf War Veterans on active duty rosters as of October 1, 1994, were identified (n = 211 642) and compared with veterans who had separated from military service and then assessed for attrition at three-year intervals during a 10-year follow-up period, examining demographic and military service characteristics, Gulf War exposure variables, and hospitalization data. Cox proportional hazard modeling was used to evaluate independent predictors of all-cause hospitalization among those still on active duty and to estimate cumulative probability of hospitalization, 1994-2004, by service branch.

RESULTS: Members of our 1994 active duty cohort were more likely to be officers, somewhat older, and married compared with those who had separated from the military after serving in the 1991 Gulf War. Selected war-related exposures or experiences did not appear to influence separation with the exception of in-theater presence during the brief ground combat phase. Overall the top three diagnostic categories for hospitalizations were musculo-skeletal, injury and poisoning, and digestive disorders. Diseases of the circulatory system and symptoms, signs, and ill-defined conditions increased proportionately over time. In-theater hospitalization was the only significant independent predictor of long-term hospitalization risk among selected war-related exposures or experiences examined. The cumulative probability of hospitalization was highest for Army and lowest for Marines. CONCLUSION: Our results were generally consistent with a previous hospitalization study of US Gulf War Veterans for the period August 1991 to July 1999. Although lack of a comparison group for our study limits interpretation of overall findings, intra-cohort analyses showed no significant associations between long-term hospitalization and war-related exposures or experiences, with the exception of in-theater hospitalization, within our active duty subset of 1991 Gulf War Veterans.

Horner RD, Grambow SC, Coffman CJ, Lindquist JH, Oddone EZ, Allen KD, Kasarskis EJ (2008) Amyotrophic lateral sclerosis among 1991 Gulf War veterans: evidence for a time-limited outbreak. Neuroepidemiology 31:28-32.

BACKGROUND: In follow-up to recent reports of an elevated risk of amyotrophic lateral sclerosis (ALS) among 1991 Gulf War Veterans, we analyzed the distribution of disease onset times to determine whether the excess risk was time limited. METHODS: This secondary analysis used data from a population-based series of ALS cases identified between 1991 and 2001 among the 2.5 million military personnel who were on active duty during the 1991 Gulf War. Annual standardized incidence ratios (SIR) were calculated for all cases and for those with disease onset before age 45 years. RESULTS: Forty-eight of 124 cases occurred among those deployed to the Persian Gulf region during the war. The annual SIR for deployed military personnel did not demonstrate a monotonically increasing trend for either all cases ($\chi^2 = 0.11$, d.f. = 1, $p = 0.74$) or for cases under 45 years of age at onset ($\chi^2 = 2.41$, d.f. = 1, $p = 0.12$). The highest risk was observed in 1996, declining thereafter. Among military personnel who were not deployed to the Gulf region, the level of risk remained fairly constant during the 11-year period. CONCLUSIONS: The excess risk of ALS among 1991 Gulf War Veterans was limited to the decade following the war.

Inman AO, Monteiro-Riviere NA, Riviere JE (2008) Inhibition of jet fuel aliphatic hydrocarbon induced toxicity in human epidermal keratinocytes. J Appl Toxicol 28:543-553.

Jet propellant (JP)-8, the primary jet fuel used by the U.S. military, consists of hydrocarbon-rich kerosene base commercial jet fuel (Jet-A) plus additives DC1-4A, Stadis 450 and diethylene glycol monomethyl ether. Human epidermal keratinocytes (HEK) were exposed to JP-8, aliphatic hydrocarbon (HC) fuel S-8 and aliphatic HC pentadecane (penta), tetradecane (tetra), tridecane (tri) and undecane (un) for 5 min. Additional studies were conducted with signal transduction pathway blockers parthenolide (P; 3.0 μm), isohelenin (I; 3.0 μm), SB 203580 (SB; 13.3 μm), substance P (SP; 3.0 μm) and recombinant human IL-10 (rHIL-10; 10 ng/ml). In the absence of inhibitors, JP-8 and to a lesser extent un and S-8, had the greatest toxic effect on cell viability and inflammation suggesting, as least in vitro, that synthetic S-8 fuel is less irritating than the currently used JP-8. Each inhibitor significantly ($P < 0.05$) decreased HEK viability. DMSO, the vehicle for P, I and SB, had a minimal effect on viability. Overall, IL-8 production was suppressed at least 30% after treatment with each inhibitor. Normalizing data relative to control indicate which inhibitors suppress HC-mediated IL-8 to control levels. P was the most effective inhibitor of IL-8 release; IL-8 was significantly decreased after exposure to un, tri, tetra and penta but significantly increased after JP-8 exposure compared with controls. Inhibitors were not effective in suppressing IL-8 release in JP-8 exposures to control levels. This study shows that inhibiting NFκ B, which appears to play a role in cytokine production in HC-exposed HEK in vitro, may reduce the inflammatory effect of HC in vivo.

Johnson EA, Daugherty KS, Gallagher SJ, Moran AV, DeFord SM (2008) Glutamate receptor pathology is present in the hippocampus following repeated sub-lethal soman exposure in the absence of spatial memory deficits. Neurotoxicology 29:73-80.

Much is still unknown about the long-term effects of repeated, sub-lethal exposure to organophosphorus (OP) nerve agents, such as soman (GD), on learning and memory tasks and related protein expression in the hippocampus. In the present study, guinea pigs were exposed to sub-lethal doses of GD for 10 days and cognitive performance assessed using the Morris water maze (MWM) up to 88 days post-exposure to investigate spatial learning. Additionally, hippocampal lysates were probed for cytoskeletal, synaptic and glutamate receptor proteins using Western blot analyses. No significant difference in MWM performance was observed between repeated sub-lethal GD exposed and saline control groups. However, Western blot analyses revealed significant changes in glutamate receptor protein immunoreactivity for subunits GluR2, NMDAR1, NMDAR2a and NMDAR2b in the hippocampi of GD-exposed

guinea pigs. Levels of GluR2, NMDAR2a and NMDAR2b increased by 3 months post-initial exposure and returned to control levels by 6 months while NMDAR1 decreased by 6 months. No significant differences in neurofilament medium (NFM), neurofilament light (NFL) or synaptophysin densitometry were detected and α-II-spectrin proteolytic breakdown was also absent. These results reveal that repeated, sub-lethal exposure to GD affects glutamate receptor subunit expression but does not affect cytoskeletal protein immunoreactivity or the proteolytic state in the hippocampus. Though these changes do not affect spatial memory, they may contribute to other cognitive deficits previously observed following sub-lethal OP exposure.

Kaur P, Radotra B, Minz RW, Gill KD (2007) Impaired mitochondrial energy metabolism and neuronal apoptotic cell death after chronic dichlorvos (OP) exposure in rat brain. Neurotoxicology 28:1208-1219.
The present study elucidates a possible mechanism by which chronic organophosphate exposure (dichlorvos 6 mg/kg bw, s.c. for 12 weeks) causes neuronal degeneration. Mitochondria, as a primary site of cellular energy generation and oxygen consumption represent itself a likely target for organophosphate poisoning. Therefore, the objective of the current study was planned with an aim to investigate the effect of chronic dichlorvos exposure on mitochondrial calcium uptake, oxidative stress generation and its implication in the induction of neuronal apoptosis in rodent model. Mitochondrial preparation from dichlorvos (DDVP) treated rat brain demonstrated significant increase in mitochondrial Ca(2+) uptake (644.2 nmol/mg protein). Our results indicated decreased mitochondrial electron transfer activities of cytochrome oxidase (complex IV) along with altered mitochondrial complex I, and complex II activity, which might have resulted from elevated mitochondrial calcium uptake. The alterations in the mitochondrial calcium uptake and mitochondrial electron transfer enzyme activities in turn might have caused an increase in malondialdehyde, protein carbonyl and 8-hydroxydeoxyguanosine formation as a result of enhanced lipid peroxidation, and as well as protein and mtDNA oxidation. All this could have been because of enhanced oxidative stress, decreased GSH levels and also decreased Mn-SOD activity in the mitochondria isolated from dichlorvos treated rat brain. Thus, chronic organophosphate exposure has the potential to disrupt cellular antioxidant defense system which in turn triggers the release of cytochrome c from mitochondria to cytosol as well as caspase-3 activation in dichlorvos treated rat brain as revealed by immunoblotting experiments. Low-level long-term organophosphate exposure finally resulted in oligonucleosomal DNA fragmentation, a hallmark of apoptosis. These studies provide an evidence of impaired mitochondrial bioenergetics and apoptotic neuronal degeneration after chronic low-level exposure to dichlorvos.

Kelsall H, McKenzie D, Sim M, Leder K, Ross J, Forbes A, Ikin J (2008) Comparison of self-reported and recorded vaccinations and health effects in Australian Gulf War veterans. Vaccine 26:4290-4297.
BACKGROUND: Vaccinations and multiple vaccinations in particular, have been associated with adverse health effects in veterans of the 1990/1991 Gulf War. However, exposure assessment has usually been based on self-report and recall bias may have influenced the results. METHODS: We investigated agreement between self-reported and recorded vaccinations and the relationship with health status in Australian Gulf War Veterans. RESULTS: Agreement between self-reported and recorded vaccinations was highest for plague (kappa=0.80), and kappa coefficients were greater than 0.60 for polio and 'other unlisted' vaccines, between 0.41 and 0.60 for hepatitis B, hepatitis A, typhoid and pertussis, and less than 0.40 for the other listed vaccines. The associations of increasing number of self-reported vaccinations in dose response relationships with total number of symptoms, functional impairment, and poorer physical health were not observed when based on recorded vaccination data, although the actual difference in estimates was small and statistically significant only for total number of symptoms. CONCLUSIONS: Vaccinations were not associated with adverse health effects when exposure assessment was based on recorded vaccinations. It would be prudent that future research studies should be based on recorded vaccination data.

Kilshaw S (2008) Gulf war syndrome: a reaction to psychiatry's invasion of the military? Cult Med Psychiatry 32:219-237.
Following the 1991 Gulf War, a number of soldiers who fought there began to complain of various symptoms and disorders, the collection of which came to be known as Gulf War syndrome (GWS). A debate has raged about the nature and cause of this illness, with many suggesting that it is a psychiatric condition. GWS continues to be a contested illness, yet there is no disputing that many Gulf veterans are ill. This article considers the way in which GWS sufferers understand their illness to be physical in nature and the way in which they negotiate and resist psychological theories of their illness. Based on 14 months of ethnographic fieldwork in the United Kingdom, data for this article were collected mainly by in-depth, semistructured interviews with GWS sufferers, their family members, doctors, and scientists, as well as healthy Gulf veterans. A total of 93 informants were interviewed, including 67 UK Gulf veterans, most of whom were ill. The paper argues that despite the increasing presence of psychiatry in military discourse, GWS reveals the way that people are able to transform, negotiate and even negate its power and assumptions.

Kim SH, Kim DH, Oh DH, Clauw DJ (2008) Characteristic electron microscopic findings in the skin of patients with fibromyalgia--preliminary study. Clin Rheumatol 27:407-411.
This blinded study was done to determine if there are any abnormal electron microscopic (EM) findings in the skin of fibromyalgia syndrome (FMS) patients, which might contribute to or be due to the increased pain sensitivity seen in this condition. Skin biopsy samples were obtained from 13FMS patients and 5 control subjects. All tissues were prepared for EM examination by immediate prefixation in 2.5% glutaraldehyde for 2 h and postfixation in 1% osmium acid for 24 h. Ultrathin sections on grids were stained by uranylacetate and lead citrate. Biopsies were read by an individual without knowledge of participant status. Five skin biopsies from healthy controls showed relatively even distribution of variegated sized unmyelinated axons sheathed well by complicatedly folded Schwann cell membranes. In tissues from 9/13 FMS patients, unmyelinated Schwann cells were noted to be ballooned, whereas this finding was not noted in any controls ($p=0.029$). Axons in most patients trended towards being localized in the periphery of the unmyelinated Schwann cell sheaths ($p=0.002$). Particularly, peripheral localization of axon in the unmyelinated Schwann cell sheath had a strong relationship with ballooning of Schwann cell ($p=0.042$), simplified folding of Schwann cell sheath ($p=0.039$) and smaller axon ($p=0.034$). Myelinated nerve fibers were unremarkable. The EM findings seen in the skin of FMS patients show unusual patterns of unmyelinated nerve fibers as well as associated Schwann cells. If these findings are replicated in a larger study, these abnormalities may contribute to, or be due to, the lower pain threshold seen in FMS patients.

King LA, King DW, Bolton EE, Knight JA, Vogt DS (2008) Risk factors for mental, physical, and functional health in Gulf War veterans. J Rehabil Res Dev 45:395-407.
Risk factors associated with war-zone events and circumstances are implicated in the health and adjustment of military veterans. We assessed a national stratified sample of community-residing veterans of the Gulf War ($N = 357$) using scales from the Deployment Risk and Resilience Inventory, along with an array of mental (posttraumatic stress disorder, depression, and anxiety), physical (symptom and condition indicators especially pertinent to Gulf War illnesses), and functional (both mental and physical dimensions) health outcomes. We found that perceived threat or fear of bodily harm in the war zone and self-reported or perceived exposures to environmental hazards may play a critical role in all measured aspects of health. Moreover, a synergistic effect of these two risk factors was observed in the prediction of mental health and mental health functional status.

Kou J, Bloomquist JR (2007) Neurotoxicity in murine striatal dopaminergic pathways following long-term application of low doses of permethrin and MPTP. Toxicol Lett 171:154-161.
The long-term effects of permethrin (PM) and its interaction with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) on striatal dopaminergic pathways were investigated in C57BL/6 mice. In a 3-month exposure, technical PM (1.5mg/kg) was administered once per week, with MPTP (20mg/kg) given once on either the 7th week or 11th week. In a 6-month exposure, PM (0.8mg/kg or 1.5mg/kg) was administered once per week for 26 weeks, with MPTP (20mg/kg) given once, on week 24. Alterations in the expression of tyrosine hydroxylase (TH), dopamine transporter (DAT), and α-synuclein proteins were analyzed 1 day after the last PM treatment using western blot assay. PM had no significant effect on striatal dopaminergic pathways by itself, whereas MPTP significantly reduced the expression of TH and DAT proteins. In both exposure paradigms, weekly 1.5mg/kg PM treatments antagonized the toxic effect of MPTP on TH and DAT expression ($p<0.05$). There was no significant alteration of α-synuclein expression following any exposure to PM and/or MPTP. [^{3}H]Tetrabenazine (TBZ) binding assay for expression of striatal vesicular monoamine transporter (VMAT) showed no effect of PM, but the reduction in this protein caused by MPTP was attenuated by PM, consistent with effects on other dopaminergic biomarkers. The overall findings demonstrate that long-term, low-dose exposure to PM alone did not cause signs of neurotoxicity to striatal dopaminergic neural terminals, or enhance the effects of MPTP. We conclude that under typical use conditions, PM poses little Parkinsonian hazard to humans, including when impregnated into clothing for control of biting flies.

Lagorio S, Grande E, Martina L (2008) [Review of epidemiological studies of cancer risk among Gulf War and Balkans veterans]. Epidemiol Prev 32:145-155.
OBJECTIVE: Analysis of the available epidemiological evidence on cancer risk among Gulf war and Balkans veterans. DESIGN AND SETTING: Eligible for the review were all studies published in peer-reviewed journals indexed in MedLine by the end of 2007. The review includes twelve studies published between 1996 and 2006 All of them are retrospective cohort studies focused on different outcomes: mortality, hospitalizations or cancer incidence. The study populations are from US, UK, Sweden, Denmark and Italy. The description of the studies reviewed focuses on their main features (design, study population, health outcomes and ascertainment procedures, analytical methods). RESULTS: Results are summarized by cancer site: all cancers, neoplasms that may be a target of exposure to depleted uranium (lung cancer, leukemias, kidney cancer, bone cancer), and other neoplasms (lymphomas, brain cancer, and

cancer of the testis) relatively frequent among young adults. The overall incidence of cancers is not increased in the cohort studies of Gulf war and Balkans veterans published to date, nor is there consistent evidence of excess risks of neoplasms possibly related to exposure to depleted uranium. However, in the Danish cohort of Balkans veterans an increased risk of bone cancer has been observed, but the excess disappeared when a 1-year latency was considered. An increased brain cancer risk in relation to exposure to nerve-gas agents has been observed. Sporadic excesses of Hodgkin lymphoma and testicular cancer in deployed veterans have been reported. CONCLUSION: None of the studies reviewed could objectively assess exposures to depleted uranium or to other potentially carcinogenic agents experienced in the theaters. The study cohorts are young and the follow-up periods are probably too short to capture excesses of long latency outcomes. The update of the follow-up of the cohorts and studies of other cohorts with a better assessment of exposure to depleted uranium and to other potentially relevant risk factors are warranted.

Li WB, Gerstmann UC, Hollriegl V, Szymczak W, Roth P, Hoeschen C, Oeh U (2008) Radiation dose assessment of exposure to depleted uranium. J Expo Sci Environ Epidemiol.
Depleted uranium (DU) is claimed to contribute to human health problems, known as the Gulf War Syndrome and the Balkan Syndrome. Quantitative radiation dose is required to estimate the health risk of DU materials. The influences of the solubility parameters in the human alimentary tract and the respiratory tract systems and the aerosol particles size on the radiation dose of DU materials were evaluated. The dose conversion factor of daily urinary excretion of DU is provided. The retention and excretion of DU in the human body after a contamination at a wound site were predicted. Dose coefficients of DU after ingestion and inhalation were calculated using the solubility parameters of the DU corrosion products in simulated gastric and simulated lung fluid, which were determined in the Helmholtz Zentrum Munchen. ^{238}U is the main radiation dose contributor per 1 Bq of DU materials. The dose coefficients of DU materials were estimated to be 3.5×10^{-8} and 2.1×10^{-6} Sv/Bq after ingestion and inhalation for members of the public. The ingestion dose coefficient of DU materials is about 75% of the natural uranium value. The inhalation dose coefficient of DU material is in between those for Type M and Type S according to the category for inhaled materials defined by the International Commission on Radiological Protection. Radiation dose possibly received from DU materials can directly be estimated by using the dose conversion factor provided in this study, if daily urinary excretion of DU is measured. Journal of Exposure Science and Environmental Epidemiology advance online publication, 2 July 2008; doi:10.1038/jes.2008.40.

Lukaszewicz-Hussain A (2008) Subchronic intoxication with chlorfenvinphos, an organophosphate insecticide, affects rat brain antioxidative enzymes and glutathione level. Food Chem Toxicol 46:82-86.
Organophosphate pesticides (OP) belong to the class of xenobiotics that are intentionally released to the environment. Toxicity of these compounds is mainly due to inhibition of acetylcholinesterase (AChE), but many authors postulate that OP in acute as well as in chronic intoxication disturb the redox processes, changing the activities of antioxidative enzymes and causing enhancement of lipid peroxidation in many organs. Epidemiological studies have demonstrated a relationship of certain human diseases with pesticide exposure and with changes in antioxidative enzymes. There is also evidence that oxidative stress is an important pathomechanism of neurological disorders such as Alzheimer disease and Parkinson disease, cardiovascular disorders and many others. The study objective was to investigate the activities of brain antioxidative enzymes and reduced glutathione level in rats subchronically intoxicated with chlorfenvinphos. In the rat brain the activities of such enzymes as superoxide dismutase, catalase, glutathione peroxidase and reductase were found to increase, while reduced glutathione level decreased in chlorfenvinphos intoxication. Based on experimental findings of this study, it can be suggested that subchronic administration of chlorfenvinphos leads to a change in the brain oxidative status and that the change occurs at a dose of 0.3 mg/kg/day, i.e., twice smaller than LOAEL level for rats.

Mach M, Grubbs RD, Price WA, Nagaoka M, Dubovicky M, Lucot JB (2008) Delayed behavioral and endocrine effects of sarin and stress exposure in mice. J Appl Toxicol 28:132-139.
The organophosphorus agent sarin is a potent inhibitor of acetylcholinesterase. Experiments tested the influence of exposure to low doses of sarin along with psychological stress on delayed behavioral and endocrine changes in mice. Motor activity, acoustic startle response (ASR), pre-pulse inhibition (PPI) of ASR, activity of cholinesterase in blood and catecholamine levels in adrenals were evaluated after low dose sarin exposure (3×0.4 LD_{50} subcutaneously) combined with chronic intermittent stress in C57BL/6J mice. While sarin alone produced depression of motor activity, no interaction of the stress with sarin exposure was observed. Cholinesterase activity was significantly reduced 24 h after exposure to sarin; however, the basal activity was re-established 3 weeks later. The combination of low dose sarin exposure and stress produced delayed behavioral change manifested as excessive grooming together with endocrine alterations in adrenals 7 weeks after exposure. The size of the adrenals in the combined exposure group was increased

and the concentration of catecholamines was significantly decreased. In conclusion, these findings indicate that sarin in low doses is more dangerous when combined with shaker stress inducing delayed behavioral and endocrine changes.

Marshall AC (2008) Gulf war depleted uranium risks. J Expo Sci Environ Epidemiol 18:95-108.
US and British forces used depleted uranium (DU) in armor-piercing rounds to disable enemy tanks during the Gulf and Balkan Wars. Uranium particulate is generated by DU shell impact and particulate entrained in air may be inhaled or ingested by troops and nearby civilian populations. As uranium is slightly radioactive and chemically toxic, a number of critics have asserted that DU exposure has resulted in a variety of adverse health effects for exposed veterans and nearby civilian populations. The study described in this paper used mathematical modeling to estimate health risks from exposure to DU during the 1991 Gulf War for both US troops and nearby Iraqi civilians. The analysis found that the risks of DU-induced leukemia or birth defects are far too small to result in an observable increase in these health effects among exposed veterans or Iraqi civilians. The analysis indicated that only a few (approximately 5) US veterans in vehicles accidentally targeted by US tanks received significant exposure levels, resulting in about a 1.4% lifetime risk of DU radiation-induced fatal cancer (compared with about a 24% risk of a fatal cancer from all other causes). These veterans may have also experienced temporary kidney damage. Iraqi children playing for 500 h in DU-destroyed vehicles are predicted to incur a cancer risk of about 0.4%. In vitro and animal tests suggest the possibility of chemically induced health effects from DU internalization, such as immune system impairment. Further study is needed to determine the applicability of these findings for Gulf War exposure to DU. Veterans and civilians who did not occupy DU-contaminated vehicles are unlikely to have internalized quantities of DU significantly in excess of normal internalization of natural uranium from the environment.

Matias-Guiu J, Garcia-Ramos G, Galan L, Vela A, Guerrero A (2008) [Analytic epidemiological information of amyotrophic lateral sclerosis]. Neurologia 23:168-178.
INTRODUCTION: The analytical epidemiological information on amyotrophic lateral sclerosis (ALS) is extensive and is based on case-control studies, selective patient series and few cohort studies that analyze the risk factors for the disease. REVIEW: The studies found in the literature on analytical epidemiology have been reviewed in an attempt to analyze the methodology, compare their results and comment on the possible biases and confounding factors such as the different roles of the risk factors. CONCLUSION: In spite of the extensive information available, the analytical epidemiology of ALS has still not clarified the etiological factors of the disease. This may be due to the influence of the genetic factors, but also to the variability of the methodological designs. However, the analytical factor that has the greatest consistency is that of exhibition to heavy metals. Greater physical activity or increased frequency in special situations such as is the cases from the first Gulf War could be suggested as a more than casual precipitating factor.

McLaughlin R, Nielsen L, Waller M (2008) An evaluation of the effect of military service on mortality: quantifying the healthy soldier effect. Ann Epidemiol 18:928-936.
PURPOSE: The healthy soldier effect denotes the proposition that military populations are likely to be healthier than other populations. A systematic review was conducted which aimed to quantify the magnitude of the healthy soldier effect. METHODS: Studies containing mortality rates of military personnel were identified from multiple electronic databases. Studies were included in the meta-analyses if they reported all-cause, cancer, or external-cause mortality in a military population and compared the rates to the general population. Fifty-nine studies were initially identified and 12 were included in the meta-analyses. RESULTS: The overall meta-standardized mortality ratios (SMRs) for all-cause mortality for deployed veterans was 0.76 (95% confidence interval [CI]: 0.65-0.89) and 0.73 (95% CI: 0.56-1.97) for non-deployed veterans based on a mean follow-up of 7.0 and 2.4 years, respectively; for cancer mortality, the SMRs were 0.78 (95% CI: 0.63-0.98) for deployed veterans and 0.75 (95% CI: 0.50-1.14) for non-deployed veterans based on 6.7 and 3.1 years follow-up, respectively; for external-cause mortality, the SMRs were 0.90 (95% CI: 0.72-1.13) for deployed veterans and 0.80 (95% CI: 0.63-1.01) for non-deployed veterans based on 4.8 and 2.0 years follow-up, respectively. CONCLUSION: Military personnel do display a healthy soldier effect that decreases their risk of mortality compared to the general population. The overall healthy soldier effect estimated ranges from 10% to 25%, depending on the cause of death studied and the period of follow-up.

Miller BG, Colvin AP, Hutchison PA, Tait H, Dempsey S, Lewis D, Soutar CA (2008) A normative study of levels of uranium in the urine of British Forces personnel. Occup Environ Med 65:398-403.
OBJECTIVES: The UK Ministry of Defence (MoD) controls a biological monitoring programme that includes testing for uranium in personnel who served in the conflict in Iraq in 2003. To help interpret the results, the MoD commissioned this study to quantify a normative reference distribution of urinary uranium concentrations in military personnel who had not served in that conflict. METHODS: The study selected and visited various military establishments to recruit a representative mix of ranks, genders and occupational groups (combat, support and auxiliary). A standardised protocol and recruitment questionnaire were used. The 125 ml spot urine samples collected

were analysed for uranium and creatinine concentrations and (where possible) for uranium isotope $^{238}U/^{235}U$ ratio. RESULTS: Samples from 732 eligible subjects were analysed. Adjusted uranium concentrations ranged up to 556 ng/g creatinine, somewhat higher than reference values quoted for the USA but much lower than recorded in granite areas such as Finland. Isotope ratio measurements were available for 125 samples (17%) with the highest concentrations; these all had a natural isotope signature and no evidence of depleted uranium (DU). On average, urinary uranium concentrations were somewhat lower in officers than in other ranks; they differed also across the services, the Navy being lowest and the Army highest. The levels give no concern regarding health risks in the personnel studied. CONCLUSION: Since even the highest values were from natural sources, we assume the differences represent differences in ingestion of natural uranium. Definition of a reference distribution or normal values will depend on the subpopulation of interest.

Miranda ML, icia Overstreet GM, Tassone E, Allen KD, Horner RD (2008) Spatial analysis of the etiology of amyotrophic lateral sclerosis among 1991 Gulf War veterans. Neurotoxicology 29:964-970.
BACKGROUND: Veterans of the 1991 Gulf War have an increased risk of amyotrophic lateral sclerosis (ALS), but the etiology is unknown. OBJECTIVES: This study sought to identify geographic areas with elevated risk for the later development of ALS among military personnel who served in the first Gulf War. METHODS: A unified geographic information system (GIS) was constructed to allow analysis of secondary data on troop movements in the 1991 Gulf War theatre in the Persian Gulf region including Iraq, northern Saudi Arabia, and Kuwait. We fit Bayesian Poisson regression models to adjust for potential risk factors, including one relatively discrete environmental exposure, and to identify areas associated with elevated risk of ALS. RESULTS: We found that service in particular locations of the Gulf was associated with an elevated risk for later developing ALS, both before and after adjustment for branch of service and potential of exposure to chemical warfare agents in and around Khamisiyah, Iraq. CONCLUSIONS: Specific geographic locations of troop units within the 1991 Gulf War theatre are associated with an increased risk for the subsequent development of ALS among members of those units. The identified spatial locations represent the logical starting points in the search for potential etiologic factors of ALS among Gulf War Veterans. Of note, for locations where the relative odds of subsequently developing ALS are among the highest, specific risk factors, whether environmental or occupationally related, have not been identified. The results of spatial models can be used to subsequently look for risk factors that follow the spatial pattern of elevated risk.

Murphy D, Hull L, Horn O, Jones M, Marteau T, Hotopf M, Rona RJ, Wessely S (2007) Anthrax vaccination in a military population before the war in Iraq: side effects and informed choice. Vaccine 25:7641-7648.
BACKGROUND: To assess any health consequences of the anthrax vaccination programme in UK Armed Forces deployed to Iraq. METHODS: Data were collected from two samples simultaneously. The first was 5302 randomly selected UK service personnel. The second was 607 service personnel involved in a longitudinal study, where pre-vaccination health had previously been collected. Both samples were offered the anthrax vaccination before they deployed to Iraq in 2003 and subsequently following their service in Iraq. Participants completed a detailed questionnaire, including a range of health outcomes, receipt of the anthrax vaccination and quality of choice. RESULTS: Seventy-two percent of the combined sample had the anthrax vaccination. Being a member of the Army, a commissioned officer or a reservist was associated with higher uptake. No differences in self-reported health were observed between those who did and did not receive the vaccination. For participants who accepted the vaccination, we found an association between making an uninformed choice and adverse health. After adjustment for baseline health in the longitudinal cohort these associations remained significant. CONCLUSIONS: Anthrax vaccination used by the UK Armed Forces in preparation for the Iraq War has not resulted in adverse health outcomes. However, of those who did accept the vaccination, reported side effects were related to whether acceptance of vaccination was perceived to be informed. Improving the quality of choice may improve self-reported ill health.

Parrish RR, Horstwood M, Arnason JG, Chenery S, Brewer T, Lloyd NS, Carpenter DO (2008) Depleted uranium contamination by inhalation exposure and its detection after approximately 20 years: implications for human health assessment. Sci Total Environ 390:58-68.
Inhaled depleted uranium (DU) aerosols are recognised as a distinct human health hazard and DU has been suggested to be responsible in part for illness in both military and civilian populations that may have been exposed. This study aimed to develop and use a testing procedure capable of detecting an individual's historic milligram-quantity aerosol exposure to DU up to 20 years after the event. This method was applied to individuals associated with or living proximal to a DU munitions plant in Colonie New York that were likely to have had a significant DU aerosol inhalation exposure, in order to improve DU-exposure screening reliability and gain insight into the residence time of DU in humans. We show using sensitive mass spectrometric techniques that when exposure to aerosol has been unambiguous and in sufficient quantity, urinary excretion of DU can be detected more than 20 years after primary DU inhalation contamination ceased, even

when DU constitutes only approximately 1% of the total excreted uranium. It seems reasonable to conclude that a chronically DU-exposed population exists within the contamination 'footprint' of the munitions plant in Colonie, New York. The method allows even a modest DU exposure to be identified where other less sensitive methods would have failed entirely. This should allow better assessment of historical exposure incidence than currently exists.

Passard A, Attal N, Benadhira R, Brasseur L, Saba G, Sichere P, Perrot S, Januel D, Bouhassira D (2007) Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia. Brain 130:2661-2670.
Non-invasive unilateral repetitive transcranial magnetic stimulation (rTMS) of the motor cortex induces analgesic effects in focal chronic pain syndromes, probably by modifying central pain modulatory systems. Neuroimaging studies have shown bilateral activation of a large number of structures, including some of those involved in pain processing, suggesting that such stimulation may induce generalized analgesic effects. The goal of this study was to assess the effects of unilateral rTMS of the motor cortex on chronic widespread pain in patients with fibromyalgia. Thirty patients with fibromyalgia syndrome (age: 52.6 +/- 7.9) were randomly assigned, in a double-blind fashion, to two groups, one receiving active rTMS (n = 15) and the other sham stimulation (n = 15), applied to the left primary motor cortex in 10 daily sessions. The primary outcome measure was self-reported average pain intensity over the last 24 h, measured at baseline, daily during the stimulation period and then 15, 30 and 60 days after the first stimulation. Other outcome measures included: sensory and affective pain scores for the McGill pain Questionnaire, quality of life (assessed with the pain interference items of the Brief Pain Inventory and the Fibromyalgia Impact Questionnaire), mood and anxiety (assessed with the Hamilton Depression Rating Scale, the Beck Depression Inventory and the Hospital Anxiety and Depression Scale). We also assessed the effects of rTMS on the pressure pain threshold at tender points ipsi- and contralateral to stimulation. Follow-up data were obtained for all the patients on days 15 and 30 and for 26 patients (13 in each treatment group) on day 60. Active rTMS significantly reduced pain and improved several aspects of quality of life (including fatigue, morning tiredness, general activity, walking and sleep) for up to 2 weeks after treatment had ended. The analgesic effects were observed from the fifth stimulation onwards and were not related to changes in mood or anxiety. The effects of rTMS were more long-lasting for affective than for sensory pain, suggesting differential effects on brain structures involved in pain perception. Only few minor and transient side effects were reported during the stimulation period. Our data indicate that unilateral rTMS of the motor cortex induces a long-lasting decrease in chronic widespread pain and may therefore constitute an effective alternative analgesic treatment for fibromyalgia.

Pastula DM, Coffman CJ, Allen KD, Oddone EZ, Kasarskis EJ, Lindquist JH, Morgenlander JC, Norman BB, Rozear MP, Sams LA, Sabet A, Bedlack RS (2008) Factors associated with survival in the National Registry of Veterans with ALS. Amyotroph Lateral Scler1-7.
The clinical course of patients with ALS is highly variable. While the median survival time from symptom onset is 2-4 years, there are reports of survival ranging from less than a year to more than 40 years. Such variability makes planning difficult for patients and physicians, and complicates clinical trial design. We sought to validate previous predictors of survival and search for new ones using a large group of ALS patients in the National Registry of Veterans with ALS. We were especially interested in how various aspects of military service might affect survival. Subjects were those in the National Registry of Veterans with ALS who had probable or definite ALS (according to El Escorial criteria). A multivariable Cox proportional hazard regression model was used to examine variables for statistical association with ventilator-free survival time (determined from date of first diagnosis). Subjects who had not died or started ventilation by 31 October 2006 were censored. Our group of 1085 US military veterans with ALS was primarily male (98%) and white (94%), with mostly sporadic (95%) and extremity-onset (76%) ALS. Symptom onset occurred at a mean age of 59.3 years (60.6 years for diagnosis). Median survival time from symptom onset was 4.7 years (3.3 years from diagnosis). In our multivariable model, older age at diagnosis (HR 1.41 (95% CI 1.27-1.55) per 10-year increase), non-extremity site of onset (HR 1.55 (1.24-1.94)), and past deployment to Vietnam (HR 1.73 (1.36-2.19)) were all associated with shortened survival. A longer time to diagnosis was associated with better survival (HR 0.77 (0.70-0.84) per one year increase in diagnosis time). In this unique cohort of veterans with ALS, traditional factors of reduced survival remained important. In addition, past deployment to Vietnam was found to be associated with shortened survival as well. This finding could be due to a common exposure, a shared characteristic, an unmeasured confounder, or an enrollment bias. More research will be needed to understand the reasons behind this new finding.

Pessler F, Chen LX, Dai L, Gomez-Vaquero C, az-Torne C, Paessler ME, Scanzello C, Cakir N, Einhorn E, Schumacher HR (2008) A histomorphometric analysis of synovial biopsies from individuals with Gulf War Veterans' Illness and joint pain compared to normal and osteoarthritis synovium. Clin Rheumatol 27:1127-1134.
We compared histologic, immunohistochemical, and vascular findings in synovial biopsies from individuals with Gulf War Veterans Illness and joint pain (GWVI) to findings in normal and osteoarthritis (OA) synovium. The following

parameters were assessed in synovial biopsies from ten individuals with GWVI: lining thickness, histologic synovitis score, and vascular density in hematoxylin & eosin-stained sections; and CD68+ lining surface cells and CD15+, CD3+, CD8+, CD20+, CD38+, CD68+, and Ki-67+ subintimal cells and von Willebrand Factor+ vessels immunohistochemically. Comparisons were made to synovial specimens from healthy volunteers (n = 10) and patients with OA or RA (n = 25 each). Histologic appearance and quantitative assessments were nearly identical in the GWVI and normal specimens. Vascular density was between 25% (H & E stains; p = 0.003) and 31% (vWF immunostains; p = 0.02) lower in GWVI and normal specimens than in OA. CD68+ macrophages were the most common inflammatory cells in GWVI (45.3 +/- 10.1 SEM cells/mm^2) and normal synovium (45.6 +/- 7.4) followed by CD3+ T cells (GWVI, 15.1 +/- 6.3; normal, 27.1 +/- 9.2), whereas there were practically no CD20+, CD38+, and CD15+ cells. All parameters except lining thickness and CD15 and CD20 expression were significantly higher in OA. Five (20%) OA specimens contained significant fractions of humoral immune cells in mononuclear infiltrates, although the overall differences in the relative composition of the OA mononuclear infiltrates did not reach statistical significance compared to GWVI and normal synovium. In summary, the GWVI and normal synovia were indistinguishable from each other and contained similar low-grade inflammatory cell populations consisting almost entirely of macrophages and T cells.

Raheja G, Gill KD (2007) Altered cholinergic metabolism and muscarinic receptor linked second messenger pathways after chronic exposure to dichlorvos in rat brain. Toxicol Ind Health 23:25-37.
Chronic dichlorvos exposure (6 mg/kg b.wt/day) for a period of 8 weeks resulted in significant reduction in body weight gain of the male Wistar rats. However, the dietary intake remained unchanged in experimental animals following dichlorvos treatment. Activity of the synthesizing enzyme of acetylcholine (ACh) ie, choline acetyltransferase, was found to be significantly increased and the activity of hydrolyzing enzyme, acetyl cholinesterase (AChE), was inhibited in all the three brain regions studied. Chronic dichlorvos treatment also caused significant reduction in both high affinity (HA) and low affinity (LA) choline uptake (CU), with maximal effect being observed in the brain stem followed by cerebellum and cerebrum. Muscarinic receptor binding was significantly decreased in brain stem and cerebellum as reflected in the decreased receptor number (B_{max}), without any change in the binding affinity (K_d) of the receptors. Dichlorvos treatment caused marked inhibition in cAMP synthesis as indicated by decreased adenylate cyclase activity as well as cAMP levels in cerebrum, cerebellum and brain stem. Our study shows that organophosphates may interact with muscarinic receptor-linked second messenger system and this could be a potential mechanism for the neurotoxic effects observed after repeated exposure to low levels of organophosphates, which are unexplainable on the basis of cholinergic hyperactivity.

Ramos G, Limon-Flores AY, Ullrich SE (2007) Dermal exposure to jet fuel suppresses delayed-type hypersensitivity: a critical role for aromatic hydrocarbons. Toxicol Sci 100:415-422.
Dermal exposure to military (JP-8) and/or commercial (Jet-A) jet fuel suppresses cell-mediated immune reactions. Immune regulatory cytokines and biological modifiers, including platelet activating factor (PAF), prostaglandin E_2, and interleukin-10, have been implicated in the pathway of events leading to immune suppression. It is estimated that approximately 260 different hydrocarbons are found in jet fuel, and the exact identity of the active immunotoxic agent(s) is unknown. The recent availability of synthetic jet fuel (S-8), which is refined from natural gas, and is devoid of aromatic hydrocarbons, made it feasible to design experiments to address this problem. Here we tested the hypothesis that the aromatic hydrocarbons present in jet fuel are responsible for immune suppression. We report that applying S-8 to the skin of mice does not upregulate the expression of epidermal cyclooxygenase-2 (COX-2) nor does it induce immune suppression. Adding back a cocktail of seven of the most prevalent aromatic hydrocarbons found in jet fuel (benzene, toluene, ethylbenzene, xylene, 1,2,4-trimethlybenzene, cyclohexylbenzene, and dimethylnaphthalene) to S-8 upregulated epidermal COX-2 expression and suppressed a delayed-type hypersensitivity (DTH) reaction. Injecting PAF receptor antagonists, or a selective cycloozygenase-2 inhibitor into mice treated with S-8 supplemented with the aromatic cocktail, blocked suppression of DTH, similar to data previously reported using JP-8. These findings identify the aromatic hydrocarbons found in jet fuel as the agents responsible for suppressing DTH, in part by the upregulation of COX-2, and the production of immune regulatory factors and cytokines.

Reiter RJ, Acuna-Castroviejo D, Tan DX (2007) Melatonin therapy in fibromyalgia. Curr Pain Headache Rep 11:339-342.
Fibromyalgia (FM) is a painful syndrome that is more common in women than in men. Whether FM has an organic basis or whether it is psychosomatic is debated. Of the numerous treatments that have been tried, rarely have any been completely effective in relieving the pain of FM. Preliminary evidence indicates that melatonin, a molecule that is endogenously produced and is available as an over-the-counter supplement, may be effective in treating the pain associated with this syndrome. Although melatonin is commonly known as a sleep aid (sleep/wake problems are

common in FM sufferers), it has a variety of other beneficial effects that may account for its potential benefits in the treatment of FM.

Sarzi-Puttini P, Buskila D, Carrabba M, Doria A, Atzeni F (2008) Treatment strategy in fibromyalgia syndrome: where are we now? Semin Arthritis Rheum 37:353-365.
INTRODUCTION: The treatment of the fibromyalgia syndrome (FMS) is not standardized and often ineffective, and the course of disease progression is unpredictable. OBJECTIVES: To highlight the efficacy of the pharmacologic and nonpharmacologic treatments administered to FMS patients. METHODS: Medline search for articles published between 1983 and 2007, using the keywords fibromyalgia, pharmacologic and nonpharmacologic treatment, and multidisciplinary modalities. RESULTS: Randomized controlled trials (RCTs) indicate that FMS has been treated by a wide range of drugs including antidepressants, opioids, nonsteroidal anti-inflammatory drugs, sedatives, muscle relaxants, and antiepileptic agents. Although the syndrome is now more widely recognized and understood, its treatment remains challenging and some physicians believe that no effective treatment exists. Only a few drugs have been shown to have clear-cut benefits in RCTs. FMS sufferers benefit from exercise and a number of the tested programs have involved more than 1 type of exercise. Two other major approaches are psychophysiologically based therapy, such as electromyography biofeedback, and interventions based on cognitive-behavioral therapy. Twelve controlled clinical studies have provided evidence supporting the efficacy of treatments administered to people with FMS by multidisciplinary teams using multicomponent strategies. CONCLUSIONS: It is difficult to draw definite conclusions concerning the most appropriate approach to managing FMS because of the methodological limitations of the available studies and the fact that the heterogeneity and nonstandardized nature of their therapeutic programs make them difficult to compare. An individually tailored multidisciplinary pharmacologic, rehabilitative, and cognitive-behavioral approach currently seems to be the most effective.

Schmidt S, Allen KD, Loiacono VT, Norman B, Stanwyck CL, Nord KM, Williams CD, Kasarskis EJ, Kamel F, McGuire V, Nelson LM, Oddone EZ (2008) Genes and Environmental Exposures in Veterans with Amyotrophic Lateral Sclerosis: the GENEVA study. Rationale, study design and demographic characteristics. Neuroepidemiology 30:191-204.
Recent reports of a potentially increased risk of amyotrophic lateral sclerosis (ALS) for veterans deployed to the 1990-1991 Persian Gulf War prompted the Department of Veterans Affairs to establish a National Registry of Veterans with ALS, charged with the goal of enrolling all US veterans with a neurologist-confirmed diagnosis of ALS. The Genes and Environmental Exposures in Veterans with ALS study (GENEVA) is a case-control study presently enrolling cases from the Department of Veterans Affairs registry and a representative sample of veteran controls to evaluate the joint contributions of genetic susceptibility and environmental exposures to the risk of sporadic ALS. The GENEVA study design, recruitment strategies, methods of collecting DNA samples and environmental risk factor information are described here, along with a summary of demographic characteristics of the participants (537 cases, 292 controls) enrolled to date.

Schur E, Afari N, Goldberg J, Buchwald D, Sullivan PF (2007) Twin analyses of fatigue. Twin Res Hum Genet 10:729-733.
Prolonged fatigue equal to or greater than 1 month duration and chronic fatigue equal to or greater than 6 months duration are both commonly seen in clinical practice, yet little is known about the etiology or epidemiology of either symptom. Chronic fatigue syndrome (CFS), while rarer, presents similar challenges in determining cause and epidemiology. Twin studies can be useful in elucidating genetic and environmental influences on fatigue and CFS. The goal of this article was to use biometrical structural equation twin modeling to examine genetic and environmental influences on fatigue, and to investigate whether these influences varied by gender. A total of 1042 monozygotic (MZ) twin pairs and 828 dizygotic (DZ) twin pairs who had completed the University of Washington Twin Registry survey were assessed for three fatigue-related variables: prolonged fatigue, chronic fatigue, and CFS. Structural equation twin modeling was used to determine the relative contributions of additive genetic effects, shared environmental effects, and individual-specific environmental effects to the 3 fatigue conditions. In women, tetrachoric correlations were similar for MZ and DZ pairs for prolonged and chronic fatigue, but not for CFS. In men, however, the correlations for prolonged and chronic fatigue were higher in MZ pairs than in DZ pairs. About half the variance for both prolonged and chronic fatigue in males was due to genetic effects, and half due to individual-specific environmental effects. For females, most variance was due to individual environmental effects.

Schur EA, Afari N, Furberg H, Olarte M, Goldberg J, Sullivan PF, Buchwald D (2007) Feeling bad in more ways than one: comorbidity patterns of medically unexplained and psychiatric conditions. J Gen Intern Med 22:818-821.

BACKGROUND: Considerable overlap in symptoms and disease comorbidity has been noted among medically unexplained and psychiatric conditions seen in the primary care setting, such as chronic fatigue syndrome, low back pain, irritable bowel syndrome, chronic tension headache, fibromyalgia, temporomandibular joint disorder, major depression, panic attacks, and posttraumatic stress disorder. OBJECTIVE: To examine interrelationships among these 9 conditions. DESIGN: Using data from a cross-sectional survey, we described associations and used latent class analysis to investigate complex interrelationships. PARTICIPANTS: 3,982 twins from the University of Washington Twin Registry. MEASUREMENTS: Twins self-reported a doctor's diagnosis of the conditions. RESULTS: Comorbidity among these 9 conditions far exceeded chance expectations; 31 of 36 associations were significant. Latent class analysis yielded a 4-class solution. Class I (2% prevalence) had high frequencies of each of the 9 conditions. Class II (8% prevalence) had high proportions of multiple psychiatric diagnoses. Class III (17% prevalence) participants reported high proportions of depression, low back pain, and headache. Participants in class IV (73% prevalence) were generally healthy. Class I participants had the poorest markers of health status. CONCLUSIONS: These results support theories suggesting that medically unexplained conditions share a common etiology. Understanding patterns of comorbidity can help clinicians care for challenging patients.

Skrabek RQ, Galimova L, Ethans K, Perry D (2008) Nabilone for the treatment of pain in fibromyalgia. J Pain 9:164-173.

A randomized, double-blind, placebo-controlled trial was conducted to determine the benefit of nabilone in pain management and quality of life improvement in 40 patients with fibromyalgia. After a baseline assessment, subjects were titrated up on nabilone, from 0.5 mg PO at bedtime to 1 mg BID over 4 weeks or received a corresponding placebo. At the 2- and 4-week visits, the primary outcome measure, visual analog scale (VAS) for pain, and the secondary outcome measures, number of tender points, the average tender point pain threshold, and the Fibromyalgia Impact Questionnaire (FIQ), were evaluated. After a 4-week washout period, subjects returned for reassessment of the outcome measures. There were no significant differences in population demographics between groups at baseline. There were significant decreases in the VAS (-2.04, $P < .02$), FIQ (-12.07, $P < .02$), and anxiety (-1.67, $P < .02$) in the nabilone treated group at 4 weeks. There were no significant improvements in the placebo group. The treatment group experienced more side effects per person at 2 and 4 weeks (1.58, $P < .02$ and 1.54, $P < .05$), respectively. Nabilone appears to be a beneficial, well-tolerated treatment option for fibromyalgia patients, with significant benefits in pain relief and functional improvement. PERSPECTIVE: To our knowledge, this is the first randomized, controlled trial to assess the benefit of nabilone, a synthetic cannabinoid, on pain reduction and quality of life improvement in patients with fibromyalgia. As nabilone improved symptoms and was well-tolerated, it may be a useful adjunct for pain management in fibromyalgia.

Smith B, Wingard DL, Ryan MA, Macera CA, Patterson TL, Slymen DJ (2007) U.S. military deployment during 2001-2006: comparison of subjective and objective data sources in a large prospective health study. Ann Epidemiol 17:976-982.

PURPOSE: Studies researching service members' health after deployment have relied on self-reported deployment history, although validity of these data remains unknown. This study compared self-reported and electronic deployment data and explored differences in functional health. METHODS: Self-reported and military deployment data were compared for more than 51,000 participants enrolled in the Millennium Cohort Study (2004-2006). Kappa statistics were used to measure agreement. Analysis of variance was used to assess functional health, as measured by the Medical Outcomes Study Short Form 36-Item Health Survey for Veterans (SF-36V). RESULTS: Of 51,741 participants who completed the initial deployment question, objective records and self-report agreed in 47,355 (92%). Agreement was substantial for deployment status, frequency, and number of deployments (kappa = 0.81, 0.71, and 0.61, respectively). Deployment start dates agreed within 1 month for 82% of participants confirmed as deployed once. Participants' Mental and Physical Component Summary scores from the SF-36V did not differ by agreement level. CONCLUSIONS: These findings indicate substantial agreement between self-reported and objective deployment information and no clinically meaningful differences in functional health for the small proportion with inconsistent deployment information. These findings should be reassuring to investigators who examine military deployment as a determinant of future health.

Smith TC, Jacobson IG, Smith B, Hooper TI, Ryan MA, Team FT (2007) The occupational role of women in military service: validation of occupation and prevalence of exposures in the Millennium Cohort Study. Int J Environ Health Res 17:271-284.

To better understand the US military's global peacekeeping and combat operations, which may expose a growing

population of American service women to challenging occupations and environments. Concordance between self-reported and electronic occupation codes for female participants in the Millennium Cohort was measured using kappa statistics. Multivariable logistic regression modeling was used to assess the odds of five self-reported potentially toxic environmental exposures or disturbing experiences among different occupational categories, while adjusting for demographic and military characteristics, including deployment. Self-reported occupations were moderately to highly reliable when compared with electronic occupation data. Active-duty and Reserve/Guard females differentially reported witnessing death or trauma and exposure to chemical or biological warfare, depleted uranium, or pesticides. Findings suggest that self-reported occupation can be used with a high degree of confidence. Occupational groups with higher odds of reporting military exposures of concern will be followed longitudinally through 2022 and prospectively compared using baseline and follow-up evaluations.

Stuart JA, Ursano RJ, Fullerton CS, Wessely S (2008) Belief in exposure to chemical and biological agents in Persian Gulf War soldiers. J Nerv Ment Dis 196:122-127.
This is the first longitudinal cohort study of Persian Gulf War US soldiers to examine belief in exposure to chemical and biological weapons before and shortly after combat. A longitudinal sample of n = 1250 male Persian Gulf War US Army soldiers were surveyed 3 to 4 months before and 6 to 10 months after the 1991 War. Six to 10 months after combat, 4.6% of the cohort believed they had been exposed to chemical and biological weapons. Adjusting for demographics only, those who reported a greater number of combat exposures (odds ratio, OR: 18.8), or higher combat stress (OR: 12.27) were more likely to believe they were exposed. Adjusting for all variables soldiers who reported higher combat stress continued to be most likely (OR: 6.58) to believe they had been exposed to chemical and biological weapons. Individuals reporting higher combat stress are at substantially greater risk of reporting they have been exposed to chemical or biological weapons.

Sutedja NA, Fischer K, Veldink JH, Van Der Heijden GJ, Kromhout H, Heederik D, Huisman MH, Wokke JJ, Van Den Berg LH (2008) What we truly know about occupation as a risk factor for ALS: A critical and systematic review. Amyotroph Lateral Scler1-19.
Occupational and environmental exposures may contribute to the risk of developing sporadic amyotrophic lateral sclerosis (ALS). To summarize the available evidence, a systematic review of the literature on occupation as a potential determinant of ALS was performed according to the MOOSE guidelines. From MEDLINE, EMBASE, CINAHL, and Cochrane databases, selected studies were methodologically appraised according to Armon's classification system for ALS risk factor studies. Each occupation studied was reclassified according to the International Standard Classification of Occupations (ISCO-88). The vote-counting method was applied to summarize the data. Of 3773 potentially relevant studies, 51 were initially included. Of these, 12 studies provided risk estimates for individual occupations - one case-control, two register-based case-control, and nine register-based cohort studies. All studies fell into Armon's level of evidence class IV, indicating methodological limitations. Due to the heterogeneity of study methodology, data could not be pooled. The vote-counting method revealed several candidate occupations: veterinarians and other health workers, athletes, hairdressers, power-production plant, electrical and military workers. However, well designed studies with standardized assessment of occupation are needed to provide a more definitive answer about exogenous risk factors of ALS.

Swoboda DA (2008) Negotiating the diagnostic uncertainty of contested illnesses: physician practices and paradigms. Health (London) 12:453-478.
In the absence of scientific consensus about contested illnesses such as Chronic Fatigue Syndrome (CFS), Multiple Chemical Sensitivities (MCS), and Gulf War Syndrome (GWS), physicians must make sense of competing accounts and develop practices for patient evaluation. A survey of 800 United States physicians examined physician propensity to diagnose CFS, MCS, and GWS, and the factors shaping clinical decision making. Results indicate that a substantial portion of physicians, including nonexperts, are diagnosing CFS, MCS, and GWS. Diagnosing physicians manage the uncertainty associated with these illnesses by using strategies that enhance bounded rationality and aid in thinking beyond current disease models. Strategies include consulting ancillary information sources, conducting analytically informed testing, and considering physiological explanations of causation. By relying on these practices and paradigms, physicians fit CFS, MCS, and GWS into an explanatory system that makes them credible and understandable to them, their patients, and the medical community. Findings suggest that physicians employ rational decision making for diagnosing contested illnesses, creating a blueprint of how illnesses lacking conclusive pathogenic and etiological explanations can be diagnosed. Findings also suggest that patients with contested illnesses might benefit from working with physicians who use these diagnostic strategies, since they help manage the complexity and ambiguity of the contested illness diagnostic process and aid in diagnosis. In addition, findings provide a window into how emerging

illnesses get diagnosed in the absence of medical and scientific consensus, and suggest that diagnosing physicians advance the legitimacy of controversial illnesses by constructing the means for their diagnosis.

Taft CT, Schumm JA, Panuzio J, Proctor SP (2008) An examination of family adjustment among Operation Desert Storm veterans. J Consult Clin Psychol 76:648-656.
This study examined interrelationships among combat exposure, symptoms of posttraumatic stress disorder (PTSD), and family adjustment in a sample of male and female Operation Desert Storm veterans (N = 1,512). In structural equation models for both male and female veterans, higher combat exposure was associated with higher PTSD symptoms, which in turn were associated with poorer family adjustment, although these indirect effects did not reach statistical significance. The model for female veterans evidenced a significant direct negative association between combat exposure and family adjustment when it statistically accounted for PTSD symptoms. When the relative impacts of separate PTSD symptom groupings were examined, those reflecting withdrawal/numbing symptoms and arousal/lack of control symptoms significantly and indirectly accounted for the negative effects of combat exposure on family adjustment. Study findings indicate a number of possible pathways through which war-zone deployments negatively impact military families and suggest several avenues for future research.

Van Den Eeede F, Moorkens G, Hulstijn W, Van HB, Cosyns P, Sabbe BG, Claes SJ (2008) Combined dexamethasone/corticotropin-releasing factor test in chronic fatigue syndrome. Psychol Med 38:963-973.
BACKGROUND: Studies of hypothalamic-pituitary-adrenal (HPA) axis function in chronic fatigue syndrome (CFS) point to hypofunction, although there are negative reports. Suggested mechanisms include a reduced hypothalamic or supra-hypothalamic stimulus to the HPA axis and enhanced sensitivity to the negative feedback of glucocorticoids. The aim of the current study was to investigate HPA axis function in CFS with the dexamethasone/corticotropin-releasing factor (Dex/CRF) test, in analogy with research in affective disorders. METHOD: Thirty-four well-characterized female CFS patients and 25 healthy control subjects participated in the low-dose Dex/CRF test. Current major depressive episode was an exclusion criterion. History of early-life stress (ELS) was assessed with the Structured Trauma Interview. RESULTS: Salivary cortisol responses after 0.5 mg Dex were lower in CFS patients than in controls (before 100 μg CRF, p=0.038; after 100 μg CRF, p=0.015). A secondary analysis revealed an influence of early-life stress and of oestrogen intake. After removal of the 10 participants who were taking an oral oestrogen, patients without a history of ELS showed lower cortisol responses than patients with ELS and controls (before CRF, p=0.005; after CRF, p=0.008). CONCLUSIONS: CFS is globally associated with reduced cortisol responses in the combined low-dose Dex/CRF test, but this effect is only clearly present in CFS patients without a history of ELS. This study provides further support for an enhanced glucocorticoid negative feedback and/or a reduced central HPA axis drive in CFS. Furthermore, it demonstrates that ELS is an important variable to consider in CFS research.

Van Den Eeede F, Moorkens G, Van HB, Cosyns P, Claes SJ (2007) Hypothalamic-pituitary-adrenal axis function in chronic fatigue syndrome. Neuropsychobiology 55:112-120.
There is evidence for a hypofunction of the hypothalamic-pituitary-adrenal (HPA) axis in a proportion of the patients with chronic fatigue syndrome (CFS), despite the negative studies and methodological difficulties. In this review, we focus on challenge studies and on the role of the HPA axis in the pathogenesis of CFS. Mild hypocortisolism, blunted adrenocorticotropin response to stressors and enhanced negative feedback sensitivity to glucocorticoids are the main findings. Several underlying mechanisms have been proposed. Currently, it is a matter of debate whether these disturbances have a primary role in the pathogenesis of CFS. However, even if the HPA axis dysfunctions are secondary to other factors, they are probably a relevant factor in symptom propagation in CFS.

Verdolin MH, Stedje-Larsen ET, Hickey AH (2007) Ten consecutive cases of complex regional pain syndrome of less than 12 months duration in active duty United States military personnel treated with spinal cord stimulation. Anesth Analg 104:1557-60, table.
Complex regional pain syndrome describes a constellation of symptoms that may involve the sympathetic nervous system. Emerging consensus recommends early intervention with spinal cord stimulation to facilitate physical therapy. Isolated case reports suggest this may be an effective treatment. Ten consecutive active duty United States military personnel with newly diagnosed complex regional pain syndrome underwent early intervention with spinal cord stimulation with favorable results, including decreased pain scores and decreased opioid intake. Six received injuries directly as a result of service in Iraq or Afghanistan. These patients also had posttraumatic stress disorder, but it did not interfere with successful pain control. Additionally, 6 of 10 patients continued on active duty.

Verret C, Jutand MA, De VC, Begassat M, sefa-Colas L, Brochard P, Salamon R (2008) Reproductive health and pregnancy outcomes among French gulf war veterans. BMC Public Health 8:141.
BACKGROUND: Since 1993, many studies on the health of Persian Gulf War Veterans (PGWVs) have been undertaken. Some authors have concluded that an association exists between Gulf War service and reported infertility or miscarriage, but that effects on PGWV's children were limited.The present study's objective was to describe the reproductive outcome and health of offspring of French Gulf War Veterans. METHODS: The French Study on the Persian Gulf War (PGW) and its Health Consequences is an exhaustive cross-sectional study on all French PGWVs conducted from 2002 to 2004. Data were collected by postal self-administered questionnaire. A case-control study nested in this cohort was conducted to evaluate the link between PGW-related exposures and fathering a child with a birth defect. RESULTS: In the present study, 9% of the 5,666 Gulf veterans who participated reported fertility disorders, and 12% of male veterans reported at least one miscarriage among their partners after the PGW. Overall, 4.2% of fathers reported at least one child with a birth defect conceived after the mission. No PGW-related exposure was associated with any birth defect in children fathered after the PGW mission. Concerning the reported health of children born after the PGW, 1.0% of children presented a pre-term delivery and 2.7% a birth defect. The main birth defects reported were musculoskeletal malformations (0.5%) and urinary system malformations (0.3%). Birth defect incidence in PGWV children conceived after the mission was similar to birth defect incidence described by the Paris Registry of Congenital Malformations, except for Down syndrome (PGWV children incidence was lower than Registry incidence). CONCLUSION: This study did not highlight a high frequency of fertility disorders or miscarriage among French PGW veterans. We found no evidence for a link between paternal exposure during the Gulf War and increased risk of birth defects among French PGWV children.

Vogt DS, Samper RE, King DW, King LA, Martin JA (2008) Deployment stressors and posttraumatic stress symptomatology: comparing active duty and National Guard/Reserve personnel from Gulf War I. J Trauma Stress 21:66-74.
The increased use of National Guard and Reserve (NG/R) military personnel in current conflicts raises the question of whether deployment experiences and their associations with posttraumatic stress symptomatology differ for active duty and NG/R military personnel. To date, very few studies are available on this topic. Moreover, it is unclear whether the impact of military status differs for women and men. We addressed these research issues in a sample of 311 female and male Gulf War I veterans. Several differences were observed in deployment stressor exposures and results based on differential associations generally suggested more negative impacts of deployment experiences for active duty women and NG/R men. The potential role of unit cohesion in explaining these findings is discussed.

Vose SC, Holland NT, Eskenazi B, Casida JE (2007) Lysophosphatidylcholine hydrolases of human erythrocytes, lymphocytes, and brain: sensitive targets of conserved specificity for organophosphorus delayed neurotoxicants. Toxicol Appl Pharmacol 224:98-104.
Brain neuropathy target esterase (NTE), associated with organophosphorus (OP)-induced delayed neuropathy, has the same OP inhibitor sensitivity and specificity profiles assayed in the classical way (paraoxon-resistant, mipafox-sensitive hydrolysis of phenyl valerate) or with lysophosphatidylcholine (LysoPC) as the substrate. Extending our earlier observation with mice, we now examine human erythrocyte, lymphocyte, and brain LysoPC hydrolases as possible sensitive targets for OP delayed neurotoxicants and insecticides. Inhibitor profiling of human erythrocytes and lymphocytes gave the surprising result of essentially the same pattern as with brain. Human erythrocyte LysoPC hydrolases are highly sensitive to OP delayed neurotoxicants, with in vitro IC_{50} values of 0.13-85 nM for longer alkyl analogs, and poorly sensitive to the current OP insecticides. In agricultural workers, erythrocyte LysoPC hydrolyzing activities are similar for newborn children and their mothers and do not vary with paraoxonase status but have high intersample variation that limits their use as a biomarker. Mouse erythrocyte LysoPC hydrolase activity is also of low sensitivity in vitro and in vivo to the OP insecticides whereas the delayed neurotoxicant ethyl n-octylphosphonyl fluoride inhibits activity in vivo at 1-3 mg/kg. Overall, inhibition of blood LysoPC hydrolases is as good as inhibition of brain NTE as a predictor of OP inducers of delayed neuropathy. NTE and lysophospholipases (LysoPLAs) both hydrolyze LysoPC, yet they are in distinct enzyme families with no sequence homology and very different catalytic sites. The relative contributions of NTE and LysoPLAs to LysoPC hydrolysis and clearance from erythrocytes, lymphocytes, and brain remain to be defined.

Williams NH, Harrison JM, Read RW, Black RM (2007) Phosphylated tyrosine in albumin as a biomarker of exposure to organophosphorus nerve agents. Arch Toxicol 81:627-639.
The organophosphorus nerve agents sarin, soman, cyclosarin and tabun phosphylate a tyrosine residue on albumin in human blood. These adducts may offer relatively long-lived biological markers of nerve agent exposure that do not 'age' rapidly, and which are not degraded by therapy with oximes. Sensitive methods for the detection of these adducts have

been developed using liquid chromatography-tandem mass spectrometry. Adducts of all four nerve agents were detected in the blood of exposed guinea pigs being used in studies to improve medical countermeasures. The tyrosine adducts with soman and tabun were detected in guinea pigs receiving therapy 7 days following subcutaneous administration of five times the LD_{50} dose of the respective nerve agent. VX also forms a tyrosine adduct in human blood in vitro but only at high concentrations.

IV. RESEARCH FUNDING TRENDS

The following section provides a quantitative overview of the current research portfolio on GWVI and the evolution of the portfolio since 1999. Topics that are covered include research expenditures by VA, DoD, and HHS from FY 1999-2008, and the number of research projects in which the Federal Government has invested.

The appropriated funds for FY 1999 through 2008, centrally obligated to each project, are shown in Appendix C and summarized in Table IV-1. Federal funding for GW research totaled approximately $273 million during this period. Funds obligated for these projects prior to FY 1999 are not shown in either Table IV-1 or Appendix C. Since many projects are multi-year efforts for which funds are obligated at the beginning of the project period, projects that received all of their funds prior to FY 1999 are listed with no associated obligation ($0) in Appendix C. Federal funds for these earlier projects were reported in prior *Annual Reports to Congress*.

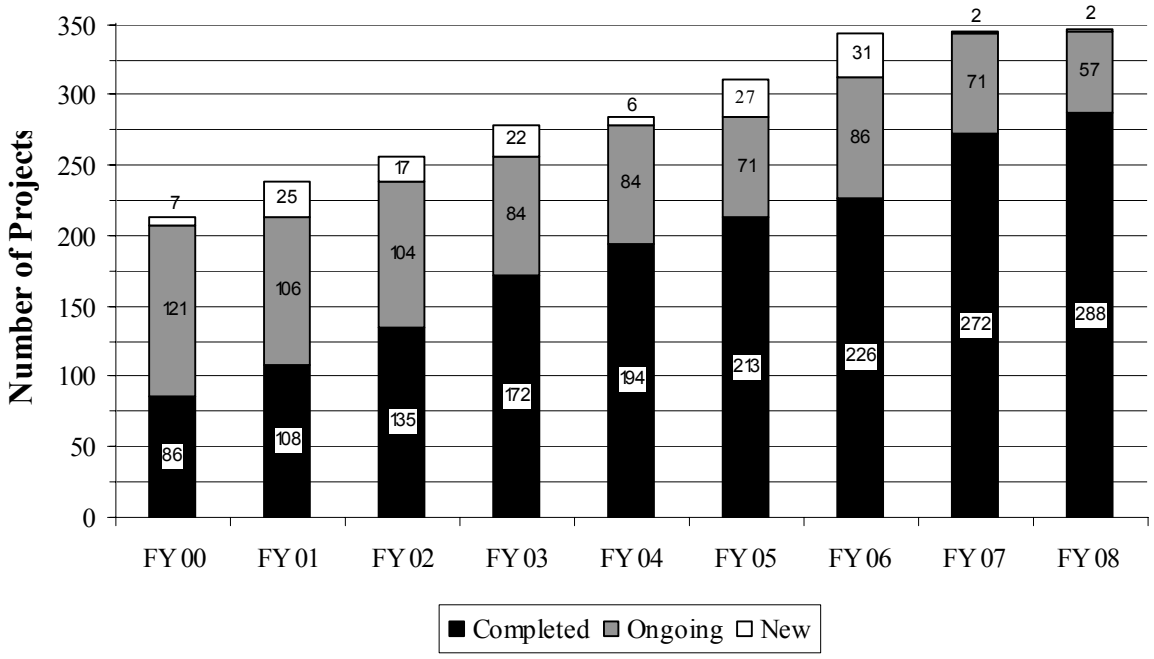
Table IV-1. 10-Year (FY 1999-2008) Funding Trends for GW Research in Millions of Dollars

Department	FY '99	FY '00	FY '01	FY '02	FY '03	FY '04	FY '05	FY '06	FY '07	FY '08	Total Costs FY '99-'08
DoD	$ 22.7	$ 23.8	$ 31.6	$ 18.8	$ 16.4	$ 11.1	$ 10.1	$ 10.1	$ 3.4	$ 3.2	**$ 151.2**
HHS	$ 1.6	$ 1.6	$ 1.0	$ 0.8	$ 1.0	$ 0.5	$ 0.5	$ 0.4	$ 0.4	$ 0.4	**$ 8.2**
VA	$ 9.0	$12.0	$ 8.6	$ 4.5	$ 5.7	$ 7.6	$ 9.5	$12.9	$ 22.0	$ 21.6	**$ 113.4**
Total	**$ 33.3**	**$ 37.4**	**$ 41.2**	**$ 24.1**	**$ 23.1**	**$ 19.2**	**$ 20.1**	**$ 23.4**	**$ 25.8**	**$ 25.2**	**$ 272.8**

VA, DoD, and HHS sponsored a total of 347 distinct research projects on GWVI during the period of FY 1992 through FY 2008. Appendix A lists all of the research and development projects and programs supported now or in the past by each of the three Federal agencies (DoD, HHS, and VA). Nine projects have been dual-funded by VA and DoD, and each agency has given the project its own unique project number (DoD-115/VA-062; DoD-116/VA-063; DoD-116A/VA-063A; DoD-116B/VA-063B; D0D-118/VA-061; DoD-119/VA-055; DoD-125/VA-074; DoD-143/VA-078; and DoD-154/VA-088). In prior *Annual Reports*, the total number of funded projects was corrected for the number of dual funded projects. Starting with the 2005 *Annual Report*, this practice has been discontinued since VA and DoD may start or end funding of their portion of these projects independent of each other. Each dual-funded project is, therefore, treated as 2 distinct projects.

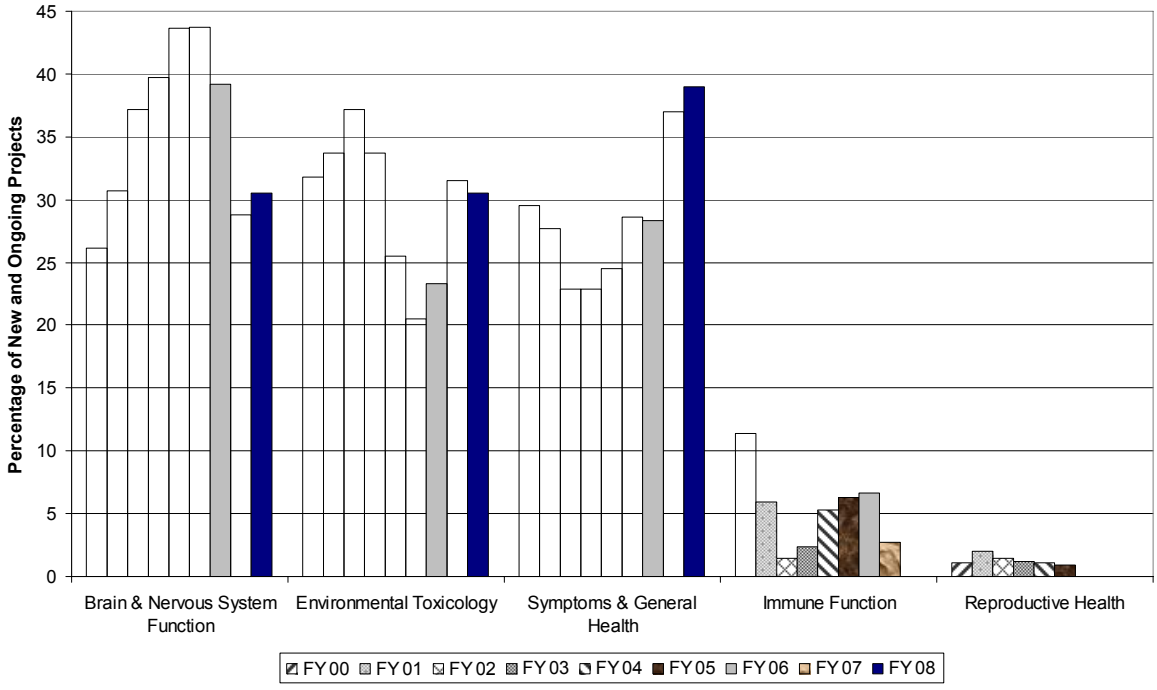
The numbers of new, ongoing and completed projects for FY 2000 - FY 2008 are shown in Figure IV-1. As of September 30, 2008, 288 projects (83 percent of the 347 projects) were completed, and 59 projects (17 percent) were new or ongoing; the numbers of new, ongoing, and completed projects for each fiscal year are shown in Figure IV-1.

Figure IV-1. Cumulative Number of Funded Projects (FY 2000 – FY2008)



The annual distribution of new and ongoing projects within the five major Research Focus Areas is shown in Figure IV-2. From FY 2000 through 2008 new and ongoing research assigned to Brain and Nervous System Function, Environmental Toxicology and General Health and Symptoms has represented 94.2 ± 1.4 percent of the new and ongoing projects.

Figure IV-2. Annual Distribution of Topic Areas for New and Ongoing Projects



V. NEW RESEARCH PROJECTS AND INITIATIVES

A. New Initiatives

VA has entered into a contractual agreement with the University of Texas Southwestern Medical Center for research related to illnesses affecting some Veterans of the Gulf War. Task orders were submitted for approval under this contract in FY 2008.

B. Portfolio Review

Funded projects in infectious diseases were closed as of FY 2006 within the Gulf War research portfolio (i.e., no funds for FY 2007 or later will be listed in Appendix C). These projects and their prior funding will remain in Appendices A, B, and C to retain continuity with previous *Annual Reports to Congress*. These projects remain open and funded, however, within the general research portfolio.

Similarly, PTSD-related projects that were included in the Federal Gulf War research portfolio in past Annual Reports were closed as of FY 2006 if they did not directly study populations of ill Gulf War Veterans or did not investigate new treatments that could prove beneficial for ill Gulf War Veterans.

C. New Projects

This section highlights the new research projects that have been approved since last year's *Annual Report to Congress*. Projects proceeded by an asterisk (*) were funded using funds appropriated in prior years or approved for funding in prior fiscal years, but were not identified in previous *Annual Reports to Congress*. They are described below and incorporated into the tables in Appendices A, B and C.

Department of Defense (DoD)

No new Gulf war-related projects were initiated in FY 2008. Projects funded through the 2008 CDMRP Gulf War Research Program did not have start dates in FY2008 and will, therefore, be reported in the 2009 Annual Report.

Department of Veterans Affairs (VA)

VA initiated funding for 2 new projects during FY 2008 focused on Brain and Nervous System Function.

VA-151, "Genetic Epidemiology of ALS" will identify genes that may confer susceptibility to the development of ALS, as well as the interplay between environmental exposures and genetic susceptibility in the development of ALS.

VA-152, "Multiple Sclerosis in Gulf War Veterans" will quantify the risk for developing MS in Gulf War Veterans deployed to the combat theater versus those not deployed, as well as the risk for developing MS in Gulf War Veterans potentially exposed to smoke from oil well fires or sarin.

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Appendices

Federally Funded Research Projects

Appendix A

Project Index By Department

DEPARTMENT OF DEFENSE PROJECTS

DoD-001	Naval Health Study Program
DoD-001A	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees
DoD-001B	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not
DoD-001C	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among Gulf War Veterans and other active-duty personnel
DoD-001D	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans
DoD-001E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
DoD-001F	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV
DoD-001G	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War Veterans
DoD-002	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET
DoD-004	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey
DoD-007A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling
DoD-007B	Carcinogenicity of Depleted Uranium Fragments
DoD-008A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL)
DoD-008B	Development of a Leishmania Skin Test Antigen (LSTA)
DoD-009	Identification of the Genetic Factors Which Control Tropism in Leishmania
DoD-010	Pyridostigmine Synergistic Toxicity Study
DoD-011	Male/Female Differential Tolerances to Pyridostigmine Bromide

DoD-013	Effects of Persian Gulf War Service on Military Working Dogs
DoD-014	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry
DoD-015	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm
DoD-016	Kuwait Oil Fire Health Risk Assessment
DoD-017	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning
DoD-018	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)
DoD-019	Persian Gulf Veterans Health Tracking System
DoD-021	Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm
DoD-022	Chronic Organophosphorus Exposure and Cognition
DoD-023	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families
DoD-030	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study
DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome
DoD-032	Neuropsychological Functioning in Persian Gulf Era Veterans
DoD-033	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity
DoD-034	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents
DoD-035	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War
DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms
DoD-037	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats
DoD-038	Diagnostic Antigens of Leishmania tropica
DoD-039	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces
DoD-040	Psychological and Neurobiological Consequences of the Gulf War Experience

DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans
DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment
DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions
DoD-045	Air Force Women's Health Surveillance Study
DoD-046	Exploratory Data Analysis with the CCEP Database
DoD-047	Study of Mycoplasmal Infections in Gulf War Veterans
DoD-048	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs Selected Control Groups
DoD-049	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts
DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways
DoD-051	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses
DoD-052	Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans
DoD-053	Long-Term Effects of Subclinical Exposures to Sarin
DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure
DoD-055	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects
DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine
DoD-057	Physiologic Effects of Stress in Gulf War Veterans
DoD-058	Illness Among Persian Gulf War Veterans: Case Validation Studies
DoD-059	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis
DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness
DoD-061	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid
DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice

DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity
DoD-064	Individual Differences in Neurobehavioral Effects of Pyridostigmine
DoD-065	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment
DoD-066	Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction
DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria
DoD-069	Five-Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents
DoD-070	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes
DoD-071	A Comparison of Post Deployment Hospitalization Between Vietnam and Gulf War Veterans
DoD-072	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals
DoD-073	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes
DoD-074	Relationship of Stress Exposures to Health in Gulf War Veterans
DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides
DoD-076	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel
DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War
DoD-078	Experimental Models of Gulf War Syndrome
DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier
DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells
DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress
DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs
DoD-083	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism
DoD-084	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD
DoD-085	CNS Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms
DoD-086	Effects of Combat Stress on Structure and Function of the Hippocampus

DoD-087	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs
DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD
DoD-089	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder
DoD-090	SPECT Benzodiazepine Receptor and MR Imaging in PTSD
DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors
DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder
DoD-093	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up
DoD-094	Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. Gulf War Veterans
DoD-095	Development of Diagnostic tools and alternative treatment drugs for Leishmania
DoD-096	Deployment Health Center
DoD-097	Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis
DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans
DoD-099	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations
DoD-100	Antibodies to Squalene
DoD-101	Mechanisms in Chronic Multisymptom Illnesses
DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans
DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala
DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity
DoD-108	Health Status of Current National Guard Members

DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms
DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy
DoD-111	Autonomic Dysfunction in Gulf War Veterans
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects
DoD-114	A Re-examination of Neuropsychological Functioning in Persian Gulf War Veterans
DoD-115	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)
DoD-116	VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V)
DoD-116A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA)
DoD-116B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB)
DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking
DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also VA-61)
DoD-119	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also VA-55)
DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents
DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development
DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys
DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys
DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin
DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74)
DoD-126	Blood-Brain Barrier Transport of Uranium
DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man

DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity
DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness
DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents
DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses
DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness
DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome
DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin
DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorous Exposure
DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure
DoD-137	Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin
DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents
DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses
DoD-140	US Department of Defense Surveillance for Neoplasms in Infancy
DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans
DoD-142	Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)
DoD-143	Millennium Cohort Study (See also VA-78)
DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces
DoD-145	Early Intervention Research Program to Enhance Soldier Resilience
DoD-146	Assessment of Toxicology Assays Methods & Chemical Exposures Among a Cohort of US Marines
DoD-147	Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications
DoD-148	Predicting operational readiness for deployed Army National Guard and Army Reserve soldiers and families

DoD-149	Longitudinal Health Study of Gulf War Veterans
DoD-150	Validation Study of Gulf War Deployment Files
DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War Veterans
DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents
DoD-153	Gulf War Illness Research
DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-88)
DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide
DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant
DoD-157	Novel Leishmania and Malaria Potassium Channels: Candidate Therapeutic Targets
DoD-158	Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission of Genetic Damage To Offspring
DoD-159	Neurotoxicity from Chronic Exposure to Depleted Uranium
DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium
DoD-161	Glutamate Receptor Aptamers and ALS
DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function
DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin
DoD-164	Efficacy of Adjunct Sleep Interventions for PTSD (EASI-PTSD)
DoD-165	Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military – BALSAM
DoD-166	A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance
DoD-167	Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure
DoD-168	Developing Biomarkers for Fibromyalgia
DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain
DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I

DoD-171	Q10 for Gulf War Veterans
DoD-172	CNDP1 Polymorphisms and Carnosine Therapy in GWI
DoD-173	A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in Gulf War Veterans with Chronic Multisymptom Illness
DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness
DoD-175	Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium
DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome
DoD-177	Randomized Trial of an Environmental Medicine Approach to Gulf War Veterans' Illness
DoD-178	Analysis of Paraoxonase Status among US Navy Gulf War Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions

DEPARTMENT OF HEALTH AND HUMAN SERVICES PROJECTS

HHS-001	Health Assessment of Persian Gulf War Veterans from Iowa
HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18
HHS-003	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and Blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires
HHS-004	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian Gulf War Veterans In Mississippi
HHS-005	Cognitive Function and Symptom Patterns in Persian Gulf Veterans
HHS-006	Defining Gulf War Illness
HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid
HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures
HHS-009	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments
HHS-010	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline
HHS-011	Deployment to the Gulf War and the Subsequent Development of Cancer
HHS-012	Genetic Epidemiology of ALS in Veterans

DEPARTMENT OF VETERANS AFFAIRS PROJECTS

VA-001	Mortality Follow-up Study of Persian Gulf Veterans
VA-002	National Health Survey of Persian Gulf Veterans
VA-002A	VA National Survey of Persian Gulf Veterans - Phase I
VA-002B	VA National Survey of Persian Gulf Veterans - Phase II
VA-002C	VA National Survey of Persian Gulf Veterans - Phase III
VA-003	Use of Roster of Veterans Who Served in Persian Gulf Area
VA-004	Boston Environmental Hazards Research Center Program
VA-004A	Evaluation of Cognitive Functioning of Persian Gulf Veterans
VA-004B	Evaluation of Neurological Functioning in Persian Gulf Veterans
VA-004C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance
VA-004D	Evaluation of Respiratory Dysfunction Among Gulf War Veterans
VA-004E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility
VA-004F	Validity of Computerized Tests
VA-005	East Orange Environmental Hazards Research Center Program
VA-005A	Health and Exposure Survey of Persian Gulf Veterans
VA-005B	Physiological and Psychological Assessments of Persian Gulf Veterans
VA-005C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans
VA-005D	Effects of Genetics and Stress on Responses to Environmental Toxins
VA-006	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research
VA-006A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)
VA-006B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)
VA-006C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)
VA-006D	DNA Damage from Chemical Agents and Its Repair (Project IV)

VA-006E	Clinical and Epidemiology Leishmania Research
VA-007	Desert Storm Reunion Survey
VA-008	Psychological Test Data of Gulf War Veterans Over Time
VA-009	Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems
VA-010	Memory and Attention in PTSD
VA-011	Neuropsychological Functioning in Veterans
VA-012	Psychological Assessment of Operation Desert Storm Returnees
VA-013	Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study
VA-015	Vaccine-Mediated Immunity Against Leishmaniasis
VA-016	Protective Immunity in Experimental Visceral Leishmaniasis
VA-017	Immunological Evaluation of Persian Gulf Veterans
VA-018	Chronic Gastrointestinal Illness in Persian Gulf Veterans
VA-020	Psychological Adjustment in Operation Desert Shield/Storm Veterans
VA-021	A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS
VA-036	Stress Symptoms and Their Causal Attribution in Desert Storm Veterans
VA-040	Musculoskeletal Symptoms in Gulf War Syndrome
VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder
VA-047	Retrospective Verification of Mustard Gas Exposure
VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance
VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction
VA-050	Neuropsychological findings in a sample of Operation Desert Storm Veterans
VA-051	Psychobiological Assessment of Desert Storm Veterans
VA-053	Spouses and Children Program
VA-054	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress

VA-055	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)
VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)
VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)
VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)
VA-059	Demonstration Treatment Program for Gulf War Veterans with Unexplained Physical Symptoms (13)
VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans
VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also DoD-118)
VA-062	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V)
VA-063	VA/DoD Core Funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D)
VA-063A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground(Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA)
VA-063B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB)
VA-064	Boston Environmental Hazards Research Center
VA-064A	Functional Neuroimaging in Lead Exposed Adults
VA-064B	Quantification and Validation of Structure-Function Relationships Through Visuospatial Test Performance
VA-064C	Development of a Structured Neurotoxicant Assessment Checklist (SNAC) for Clinical use in Veteran Populations
VA-065	San Antonio Environmental Hazards Research Center
VA-065A	Does a Variant of the Human SOD2 Gene Increase Sensitivity to Hazards?
VA-065B	The Contribution of FEN-1 to Genetic Integrity Subsequent to Oxidative Stress
VA-065C	The Importance of Hydrogen Peroxide Detoxification in Cellular Protection
VA-065D	Do Defective Gpx1 and ALDH2 Genes Increase Sensitivity to Environmental Hazards?

VA-066	Physiological Responding in Posttraumatic Stress Disorder
VA-067	Olfactory Functioning in Gulf War Veterans
VA-068	Family Study of Fibromyalgia
VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans
VA-070	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8
VA-071	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome
VA-072	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses
VA-073	Pain Sensitivity in Gulf War Veterans with Medically Unexplained Musculoskeletal Pain
VA-074	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)
VA-075	ALS and Veterans: Are Veterans at Increased Risk?
VA-076	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD
VA-077	HPA Axis Reactivity in Men and Women with Chronic PTSD
VA-078	Millennium Cohort Study (See also DoD-143)
VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress
VA-081	Stress, Pro-Inflammatory Cytokines and Coping Behavior
VA-082	Pituitary Adrenal Function in People with Fatiguing Illness
VA-083	Neuropsychological Assessment of a Population-Based Sample of Persian Gulf War Veterans and Controls
VA-084	Neurobiology of Severe Psychological Trauma in Women
VA-085	Associative Learning in Veterans with and without Combat Experience
VA-086	A Clinical Trial of Magnetic Stimulation in Depression
VA-087	Improving Outcomes of Depression in Primary Care
VA-088	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also DoD-154)
VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis

VA-090	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness
VA-090A	Neuronal Hyperexcitability and Motor Neuron Regeneration
VA-090B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders
VA-090C	Developmental Differences in Alcohol Withdrawal Sensitivity
VA-090D	Seizures and Neuroplasticity: Physiology and Biochemistry
VA-091	The Role of Dietary Choline in Neuroprotection
VA-092	Acetylcholinesterase Activity in Gulf War Veterans
VA-093	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans
VA-094	The Immunology of Chronic Cutaneous Leishmaniasis
VA-095	The Role of Signal Regulatory Proteins in Astrocytomas
VA-096	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain
VA-097	Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas
VA-098	Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas
VA-099	Vaccination Against Visceral Leishmaniasis with a Multi-Epitope Vaccine
VA-100	Studies of the Blood-Brain Barrier and it's Manipulation
VA-101	Biomarkers Discovery in ALS
VA-102	Cholinergic and Monoaminergic Influences on Sleep
VA-103	Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal
VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome
VA-105	Expression of the Major Surface Protease of Leishmania Chagasi
VA-106	Interoceptive Stressor Conditioning: A Model for Gulf War Illness
VA-107	Evaluation of Stress Response Systems in Gulf War Veterans with CMI
VA-108	Telemedicine Treatment for Veterans with Gulf War Illness
VA-109	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics

VA-110	Pain Among Gulf War Veterans: Secondary Analysis of CSP#458 Data
VA-111	T-Cell Responses to Multiple Immunizations and Stress
VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium
VA-113	Novel Cause of Motor Neuron Disease
VA-114	Strategies in Therapeutic Development of Neurodegenerative Diseases
VA-115	Autonomic System Changes Cause Intestinal Symptoms in Gulf War Veterans
VA-116	Quantitative Trait Genes Controlling Circadian and Sleep Behaviors
VA-117	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries
VA-118	Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004
VA-119	Patterns of Microarray Gene Expression in Gulf War Illness
VA-120	Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis
VA-121	Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders
VA-122	Role of Mitochondrial Oxidative Stress in ALS
VA-123	Interactions Between Maternal Care, Stress and Pyridostigmine Bromide
VA-124	Early Life Determinants of Vulnerability to Pyridostigmine Bromide
VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla
VA-126	Structural Magnetic Resonance Imaging in Gulf War-Era Veterans
VA-127	Interactions of the Leishmania sp. with Mammalian Cells
VA-128	MR Tracking of Stem Cells for Replacement Therapy in ALS
VA-129	Glucocorticoid Responsivity in Gulf War Veterans
VA-130	Tissue Factor and Gulf War-Associated Chronic Coagulopathies
VA-131	Neuroendocrine Regulators and Proteomics in GW Veterans with CMI
VA-132	Immunologic Mechanisms and Biomarkers in Gulf War Illness
VA-133	Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness

VA-134	Autonomic Functions of Gulf War Veterans with Unexplained Illnesses
VA-135	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue
VA-136	Central Mechanisms Modulating Visceral Sensitivity
VA-137	Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans
VA-138	Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP
VA-139	Sleep Neurobiology and Circuitry
VA-140	Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS
VA-141	Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis
VA-142	VA Gulf War Biorepository Trust
VA-143	The Role of Protein Oxidation in the Progression of ALS
VA-144	Testing the Role of Permethrin on the Progression of ALS
VA-145	Proteomic Analysis of Cellular Response to Biological Warfare Agents
VA-146	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route
VA-147	The Diagnosis and Pathogenesis of Occult Leishmaniasis
VA-148	Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation
VA-149	Behavior of Neural Stem Cells in a Rat Model of GWS
VA-150	Gulf War Veterans Illnesses' Research IDIQ Contract
VA-151	Genetic Epidemiology of ALS
VA-152	Multiple Sclerosis in Gulf War Veterans

Appendix B

Project List by Research Focus Areas

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
	Diagnosis Duty Military - BALSAM	DoD-165	Biomarkers for Amyotrophic Lateral Sclerosis in Active
	Symptoms	VA-142	VA Gulf War Biorepository Trust
	Treatment; Symptoms;	DoD-166	A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance
Environmental Toxicology	Symptoms; Exposure;	VA-064 A	Functional Neuroimaging in Lead Exposed Adults
Environmental Toxicology; Chemical Weapons	Symptoms	DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity
Immune Function	Symptoms	VA-005 B	Physiological and Psychological Assessments of Persian Gulf Veterans
Symptoms and General Health			
Symptoms and General Health	Diagnosis	DoD-032	Neuropsychological Functioning in Persian Gulf Era Veterans
Symptoms and General Health	Symptoms	DoD-040	Psychological and Neurobiological Consequences of the Gulf War Experience
Symptoms and General Health	Prevention	DoD-083	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism
Symptoms and General Health	Symptoms	DoD-084	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD
Symptoms and General Health	Symptoms	DoD-086	Effects of Combat Stress on Structure and Function of the Hippocampus
Symptoms and General Health	Symptoms	DoD-089	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder
Symptoms and General Health	Diagnosis	DoD-090	SPECT Benzodiazepine Receptor and MR Imaging in PTSD
Symptoms and General Health	Symptoms	DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness
Symptoms and General Health	Diagnosis	DoD-147	Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications
Symptoms and General Health	Symptoms	HHS-005	Cognitive Function and Symptom Patterns in Persian Gulf Veterans
Symptoms and General Health	Symptoms	VA-004	Boston Environmental Hazards Research Center Program

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	VA-004 A	Evaluation of Cognitive Functioning of Persian Gulf Veterans
Symptoms and General Health	Symptoms	VA-004 B	Evaluation of Neurological Functioning in Persian Gulf Veterans
Symptoms and General Health	Diagnosis	VA-004 F	Validity of Computerized Tests
Symptoms and General Health	Symptoms	VA-005	East Orange Environmental Hazards Research Center Program
Symptoms and General Health	Symptoms	VA-006 A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)
Symptoms and General Health	Symptoms	VA-007	Desert Storm Reunion Survey
Symptoms and General Health	Symptoms	VA-009	Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems
Symptoms and General Health	Symptoms	VA-010	Memory and Attention in PTSD
Symptoms and General Health	Symptoms	VA-011	Neuropsychological Functioning in Veterans
Symptoms and General Health	Symptoms	VA-012	Psychological Assessment of Operation Desert Storm Returnees
Symptoms and General Health	Symptoms	VA-013	Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study
Symptoms and General Health	Symptoms	VA-020	Psychological Adjustment in Operation Desert Shield/Storm Veterans
Symptoms and General Health	Symptoms	VA-021	A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS
Symptoms and General Health	Symptoms	VA-050	Neuropsychological findings in a sample of Operation Desert Storm Veterans
Symptoms and General Health	Symptoms	VA-051	Psychobiological Assessment of Desert Storm Veterans
Symptoms and General Health	Symptoms	VA-054	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress
Symptoms and General Health	Symptoms	VA-064	Boston Environmental Hazards Research Center
Symptoms and General Health	Symptoms	VA-066	Physiological Responding in Posttraumatic Stress Disorder
Symptoms and General Health	Symptoms	VA-072	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses
Symptoms and General Health	Symptoms	VA-076	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD
Symptoms and General Health	Symptoms	VA-077	HPA Axis Reactivity in Men and Women with Chronic PTSD

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	VA-083	Neuropsychological Assessment of a Population-Based Sample of Persian Gulf War Veterans and Controls
Symptoms and General Health	Symptoms	VA-084	Neurobiology of Severe Psychological Trauma in Women
Symptoms and General Health	Symptoms	VA-085	Associative Learning in Veterans with and without Combat Experience
Symptoms and General Health	Treatment	VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis
Symptoms and General Health	Symptoms	VA-093	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans
Symptoms and General Health	Treatment	VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium
Symptoms and General Health	Diagnosis	VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla
Symptoms and General Health	Symptoms; Diagnosis;	DoD-065	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment
Symptoms and General Health	Symptoms; Exposure;	DoD-057	Physiologic Effects of Stress in Gulf War Veterans
Symptoms and General Health	Symptoms; Exposure;	DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome
Symptoms and General Health	Diagnosis; Symptoms;	DoD-087	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs
Symptoms and General Health	Treatment; Symptoms;	DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74)
Symptoms and General Health	Diagnosis; Symptoms;	DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses
Symptoms and General Health	Diagnosis; Symptoms;	DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces
Symptoms and General Health	Diagnosis; Symptoms;	DoD-153	Gulf War Illness Research
Symptoms and General Health	Treatment; Symptoms;	DoD-164	Efficacy of Adjunct Sleep Interventions For PTSD (EASI- PTSD)
Symptoms and General Health	Treatment; Symptoms;	VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans
Symptoms and General Health	Diagnosis; Symptoms;	VA-064 B	Quantification and Validation of Structure-Function Relationships through Visuospatial Test Performance

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Diagnosis; Symptoms;	VA-067	Olfactory Functioning in Gulf War Veterans
Symptoms and General Health	Treatment; Symptoms;	VA-074	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)
Symptoms and General Health	Treatment; Symptoms;	VA-086	A Clinical Trial of Magnetic Stimulation in Depression
Symptoms and General Health	Treatment; Symptoms;	VA-087	Improving Outcomes of Depression in Primary Care
Symptoms and General Health	Treatment; Symptoms;	VA-138	Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP
Symptoms and General Health;	Symptoms; Environmental Toxicology	VA-008	Psychological Test Data of Gulf War Veterans Over Time Exposure;

Brain and Nervous System Function

Development

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Diagnosis	VA-113	Novel Cause of Motor Neuron Disease
Symptoms and General Health	Treatment; Prevention;	VA-097	Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas
Symptoms and General Health	Diagnosis; Symptoms;	VA-101	Biomarkers Discovery in ALS
Symptoms and General Health	Treatment; Symptoms;	VA-128	MR Tracking of Stem Cells for Replacement Therapy in ALS

Brain and Nervous System Function

Epidemiology

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	DoD-023	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families
Symptoms and General Health	Symptoms	DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs
Symptoms and General Health	Symptoms	DoD-114	A Re-examination of Neuropsychological Functioning in Persian Gulf War Veterans

Brain and Nervous System Function

Epidemiology

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also VA-61)
Symptoms and General Health	Symptoms	HHS-006	Defining Gulf War Illness
Symptoms and General Health	Diagnosis	HHS-012	Genetic Epidemiology of ALS in Veterans
Symptoms and General Health	Diagnosis	VA-152	Genetic Epidemiology of ALS in Veterans
Symptoms and General Health	Symptoms	VA-036	Stress Symptoms and Their Causal Attribution in Desert Storm Veterans
Symptoms and General Health	Symptoms	VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also DoD-118)
Symptoms and General Health	Symptoms	VA-068	Family Study of Fibromyalgia
Symptoms and General Health	Symptoms	VA-075	ALS and Veterans: Are Veterans at Increased Risk?
Symptoms and General Health	Symptoms	VA-110	Pain Among Gulf War Veterans: Secondary Analysis of CSP#458 Data
Symptoms and General Health	Symptoms; Diagnosis;	DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome
Symptoms and General Health	Treatment; Prevention;	DoD-145	Early Intervention Research Program to Enhance Soldier Resilience
Symptoms and General Health	Diagnosis; Symptoms;	DoD-052	Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans
Symptoms and General Health	Diagnosis; Symptoms;	DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study
Symptoms and General Health	Diagnosis; Symptoms;	VA-088	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study
Symptoms and General Health	Diagnosis; Symptoms;	HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18

Brain and Nervous System Function

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Treatment	DoD-161	Glutamate Receptor Aptamers and ALS
	Symptoms	VA-091	The Role of Dietary Choline in Neuroprotection

Brain and Nervous System Function

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Symptoms	VA-120	Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis
	Symptoms	VA-139	Sleep Neurobiology and Circuitry
	Treatment	VA-140	Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS
	Symptoms	VA-141	Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis
Environmental Toxicology	Symptoms	VA-126	Structural Magnetic Resonance Imaging in Gulf War-Era Veterans
Environmental Toxicology	Symptoms; Exposure;	DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome
Environmental Toxicology; Symptoms and General Health	Symptoms; Exposure;	DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I
Symptoms and General Health	Symptoms	DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells
Symptoms and General Health	Symptoms	DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors
Symptoms and General Health	Symptoms	DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder
Symptoms and General Health	Symptoms	DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala
Symptoms and General Health	Symptoms	VA-081	Stress, Pro-Inflammatory Cytokines and Coping Behavior
Symptoms and General Health	Symptoms	VA-090	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War
Symptoms and General Health	Symptoms	VA-090A	Neuronal Hyperexcitability and Motor Neuron Regeneration
Symptoms and General Health	Symptoms	VA-090B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders
Symptoms and General Health	Symptoms	VA-090C	Developmental Differences in Alcohol Withdrawal Sensitivity
Symptoms and General Health	Symptoms	VA-090D	Seizures and Neuroplasticity: Physiology and Biochemistry
Symptoms and General Health	Symptoms	VA-092	Acetylcholinesterase Activity In Gulf War Veterans
Symptoms and General Health	Symptoms	VA-095	The Role of Signal Regulatory Proteins in Astrocytomas
Symptoms and General Health	Symptoms	VA-098	Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas

Brain and Nervous System Function

Mechanistic

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	VA-103	Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal
Symptoms and General Health	Symptoms	VA-109	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics
Symptoms and General Health	Treatment	VA-114	Strategies in Therapeutic Development of Neurodegenerative Diseases
Symptoms and General Health	Symptoms	VA-116	Quantitative Trait Genes Controlling Circadian and Sleep Behaviors
Symptoms and General Health	Symptoms	VA-121	Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders
Symptoms and General Health	Symptoms	VA-122	Role of Mitochondrial Oxidative Stress in ALS
Symptoms and General Health	Symptoms	VA-129	Glucocorticoid Responsivity in Gulf War Veterans
Symptoms and General Health	Treatment; Symptoms;	VA-100	Studies of the Blood-Brain Barrier and its Manipulation
Symptoms and General Health	Prevention;	VA-102	Cholinergic and Monoaminergic Influences on Sleep Symptoms

Environmental Toxicology

Clinical

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function	Interactions; Exposure; Symptoms	VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance
Brain and Nervous System Function; Symptoms and General Health	Exposure; Symptoms;	VA-005 C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans
Chemical Weapons	Symptoms	DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness

Environmental Toxicology

Clinical

Research Focus	Project Focus	Project	Project Title
Chemical Weapons	Exposure	DoD-146	Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War
Pyridostigmine Bromide	Exposure; Prevention;	DoD-011	Male/Female Differential Tolerances to Pyridostigmine Bromide
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin

Environmental Toxicology

Clinical

Research Focus	Project Focus	Project	Project Title
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms;	DoD-064	Individual Differences in Neurobehavioral Effects of Pyridostigmine
Symptoms and General Health	Exposure; Symptoms;	VA-004 D	Evaluation of Respiratory Dysfunction Among Gulf War Veterans
Symptoms and General Health; Brain and Nervous System Function	Exposure; Symptoms;	DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant

Environmental Toxicology

Development

Research Focus	Project Focus	Project	Project Title
	Interactions; Exposure;	DoD-034	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents
	Diagnosis; Exposure;	DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin
	Exposure; Interactions;	HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures
Brain and Nervous System Function; Symptoms and General Health	Diagnosis; Exposure; Symptoms	VA-064 C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in Veteran populations
Chemical Weapons	Diagnosis	DoD-049	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts
Chemical Weapons	Exposure; Diagnosis;	DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents
Chemical Weapons	Diagnosis; Exposure;	DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways

Environmental Toxicology

Development

Research Focus	Project Focus	Project	Project Title
Chemical Weapons	Diagnosis; Exposure;	DoD-137	Low Level Exposure to Sulfur Mustard: Development of an SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin
Chemical Weapons	Diagnosis; Exposure;	DoD-167	Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure
Symptoms and General Health	Diagnosis; Exposure;	DoD-018	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)
Symptoms and General Health	Diagnosis; Exposure;	DoD-019	Persian Gulf Veterans Health Tracking System
Symptoms and General Health	Diagnosis; Exposure;	DoD-100	Antibodies to Squalene
Symptoms and General Health	Diagnosis; Exposure; Symptoms	DoD-016	Kuwait Oil Fire Health Risk Assessment

Environmental Toxicology

Epidemiology

Research Focus	Project Focus	Project	Project Title
Chemical Weapons	Exposure; Symptoms;	DoD-116 A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA)
Chemical Weapons	Exposure; Symptoms;	VA-063 A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA)
Chemical Weapons; Symptoms and General Health	Exposure; Symptoms;	DoD-069	Five Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents
Chemical Weapons; Symptoms and General Health	Exposure; Symptoms;	DoD-093	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up
Pyridostigmine Bromide	Exposure	DoD-017	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent
Pyridostigmine Bromide	Prevention; Exposure;	DoD-021	Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm
Symptoms and General Health	Symptoms	DoD-013	Effects of Persian Gulf War Service on Military Working Dogs
Symptoms and General Health	Exposure; Symptoms;	DoD-094	Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. Gulf War Veterans

Environmental Toxicology

Epidemiology

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Exposure; Symptoms;	DoD-099	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations
Symptoms and General Health	Exposure; Symptoms;	VA-003	Use of Roster of Veterans Who Served in Persian Gulf Area
Symptoms and General Health	Exposure; Symptoms;	VA-006	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Exposure; Interactions;	DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals
	Exposure; Interactions;	VA-145	Proteomic Analysis of Cellular Response to Biological Warfare Agents
	Exposure; Prevention;	HHS-003	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires
	Exposure; Prevention;	VA-004 E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility
Brain and Nervous System Function	Exposure	DoD-175	Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium
Brain and Nervous System Function	Interactions; Exposure; Symptoms	DoD-178	Analysis of Paraoxonase Status among US Navy Gulf War Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions
Brain and Nervous System Function	Exposure; Interactions;	VA-146	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route
Brain and Nervous System Function	Exposure; Prevention;	DoD-159	Neurotoxicity from Chronic Exposure to Depleted Uranium
Brain and Nervous System Function	Exposure; Symptoms;	VA-144	Testing the Role of Permethrin on the Progression of ALS

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function	Exposure; Symptoms;	VA-149	Behavior of Neural Stem Cells in a Rat Model of GWS
Brain and Nervous System Function; Chemical Weapons	Exposure; Symptoms;	DoD-022	Chronic Organophosphorus Exposure and Cognition
Brain and Nervous System Function; Immune Function	Exposure; Interactions; Symptoms	DoD-037	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats
Brain and Nervous System Function;	Exposure	DoD-126	Blood-Brain Barrier Transport of Uranium
Brain and Nervous System Function;	Exposure; Symptoms	DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity
Brain and Nervous System Function;	Exposure; Symptoms;	DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness
Brain and Nervous System Function; Pyridostigmine Bromide	Exposure; Symptoms;	VA-143	The Role of Protein Oxidation in the Progression of ALS
Brain and Nervous System Function; Symptoms and General Health	Exposure; Symptoms;	DoD-007 A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic
Chemical Weapons	Exposure; Diagnosis;	DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure
Chemical Weapons; Brain and Nervous System Function	Exposure	VA-006 D	DNA Damage from Chemical Agents and Its Repair (Project IV)
Chemical Weapons; Brain and Nervous System Function	Exposure; Diagnosis;	DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorous Exposure
Chemical Weapons; Brain and Nervous System Function	Prevention; Exposure;	DoD-051	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-055	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-061	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-072	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects
Chemical Weapons; Brain and Nervous System Function	Exposure; Symptoms;	DoD-053	Long-Term Effects of Subclinical Exposures to Sarin
Chemical Weapons; Brain and Nervous System Function	Exposure; Symptoms;	DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents
Immune Function and Infectious	Exposure; Interactions;	HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid
Immune Function	Exposure; Symptoms;	DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin
Immune Function and Infectious Diseases;	Exposure	DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys
Immune Function Pyridostigmine Bromide	Exposure; Interactions;	DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War
Immune Function Symptoms and General Health	Exposure; Symptoms;	DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents
Pyridostigmine Bromide	Prevention; Exposure;	DoD-033	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity
Pyridostigmine Bromide	Exposure; Interactions;	DoD-010	Pyridostigmine Synergistic Toxicity Study
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	DoD-002	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-078	Experimental Models of Gulf War Syndrome

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	VA-006 C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms;	DoD-059	Pyridostigmine-induced Neurodegeneration: Role of Neuronal Apoptosis
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms;	VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms;	VA-106	Interoceptive Stressor Conditioning: A Model for Gulf War Illness
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms;	VA-123	Interactions Between Maternal Care, Stress and Pyridostigmine Bromide
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms;	VA-124	Early Life Determinants of Vulnerability to Pyridostigmine Bromide
Pyridostigmine Bromide; Symptoms and General Health	Exposure; Interactions; Symptoms	VA-005 D	Effects of Genetics and Stress on Responses to Environmental Toxins
Reproductive Health;	Exposure; Symptoms;	DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development
Symptoms and General Health	Exposure	VA-065	San Antonio Environmental Hazards Research Center
Symptoms and General Health	Exposure	VA-065 A	Does a Variant of the Human SOD2 Gene Increase Sensitivity to Hazards?
Symptoms and General Health	Exposure	VA-065 B	The Contribution of FEN-1 to Genetic Integrity Subsequent to Oxidative Stress
Symptoms and General Health	Exposure	VA-065 C	The Importance of Hydrogen Peroxide Detoxification in Cellular Protection

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Exposure	VA-065 D	Do Defective Gpx1 and ALDH2 Genes Increase Sensitivity to Environmental Hazards?

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Exposure	VA-065 D	Do Defective Gpx1 and ALDH2 Genes Increase Sensitivity to Environmental Hazards?
Symptoms and General Health	Exposure; Symptoms	DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium
Symptoms and General Health;	Exposure	DoD-007 B	Carcinogenicity of Depleted Uranium Fragments
Symptoms and General Health;	Exposure; Symptoms	DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys
Symptoms and General Health;	Exposure; Symptoms;	DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man

Immune Function and Infectious Diseases

Clinical

Research Focus	Project Focus	Project	Project Title
	Diagnosis	DoD-047	Study of Mycoplasmal Infections in Gulf War Veterans
	Symptoms	DoD-048	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs Selected Control Groups
	Diagnosis	VA-147	The Diagnosis and Pathogenesis of Occult Leishmaniasis
	Diagnosis; Treatment	VA-006 E	Clinical and Epidemiology Leishmania Research
Brain and Nervous System Function	Symptoms	DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD
Brain and Nervous System Function	Symptoms	VA-017	Immunological Evaluation of Persian Gulf Veterans
Environmental Toxicology	Exposure; Interactions; Symptoms	DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War- related illness
Symptoms and General Health	Treatment; Diagnosis;	DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria
Symptoms and General Health	Symptoms; Exposure;	VA-006 B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)
Symptoms and General Health	Exposure; Interactions;	DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function
Symptoms and General Health	Exposure; Symptoms;	DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment
Symptoms and General Health	Treatment; Symptoms;	DoD-119	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also VA-55)
Symptoms and General Health	Treatment; Symptoms;	VA-055	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)

Immune Function and Infectious Diseases

Development

Research Focus	Project Focus	Project	Project Title
	Diagnosis	DoD-008 A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL)
	Diagnosis	DoD-008 B	Development of a Leishmania Skin Test Antigen (LSTA)
	Diagnosis	DoD-038	Diagnostic Antigens of Leishmania tropica
	Diagnosis	DoD-066	Testing for Mycoplasmal Infection Replicability of Nucleoprotein Gene Tracking and Forensic Polymerase Chain Reaction
	Diagnosis; Treatment;	DoD-095	Development of Diagnostic Tools and Alternative Treatment Drugs for Leishmania
Symptoms and General Health	Diagnosis	DoD-097	Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis
Symptoms and General Health	Prevention; Symptoms;	VA-099	Vaccination Against Visceral Leishmaniasis with a multi-epitope vaccine

Immune Function and Infectious Diseases

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Treatment	DoD-009	Identification of the Genetic Factors Which Control Tropism in Leishmania
	Treatment	DoD-157	Novel Leishmania And Malaria Potassium Channels: Candidate Therapeutic Targets
	Prevention	VA-015	Vaccine-Mediated Immunity Against Leishmaniasis
	Prevention	VA-016	Protective Immunity in Experimental Visceral Leishmaniasis
	Symptoms	VA-127	Interactions of the Leishmania sp. with Mammalian Cells
	Prevention; Treatment;	VA-094	The Immunology of Chronic Cutaneous Leishmaniasis
Environmental Toxicology	Exposure	DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War Veterans
Environmental Toxicology	Exposure; Interactions;	DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?
Environmental Toxicology; Pyridostigmine Bromide	Exposure; Interactions;	DoD-076	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel
Environmental Toxicology; Pyridostigmine Bromide	Exposure; Interactions; Symptoms	DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress
Symptoms and General Health	Symptoms	VA-111	T Cell Responses to Multiple Immunizations and Stress
Symptoms and General Health	Treatment; Symptoms;	VA-105	Expression of the Major Surface Protease of Leishmania Chagasi

Reproductive Health

Clinical

Research Focus	Project Focus	Project	Project Title
	Symptoms	VA-053	Spouses and Children Program
Environmental Toxicology; Chemical Weapons	Symptoms	VA-047	Retrospective Verification of Mustard Gas Exposure
Immune Function	Symptoms	DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions

Reproductive Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Prevention	DoD-001 C	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A Comparative Study of Pregnancy Outcomes among Gulf War Veterans and Other Active-Duty Personnel
	Prevention	DoD-001 D	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans
	Symptoms	DoD-001 G	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War Veterans
	Prevention; Symptoms;	DoD-035	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War
	Prevention; Symptoms;	HHS-004	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian Gulf War Veterans In Mississippi

Reproductive Health

Mechanistic

Research Focus	Project Focus	Project	Project Title
Environmental Toxicology	Exposure; Symptoms;	DoD-158	Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission Of Genetic Damage To Offspring

Symptoms and General Health

Clinical

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-001 A	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees
	Diagnosis	DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms
	Symptoms	VA-018	Chronic Gastrointestinal Illness in Persian Gulf Veterans
	Symptoms	VA-040	Musculoskeletal Symptoms in Gulf War Syndrome
	Treatment; Diagnosis; Symptoms	DoD-172	CNDP1 Polymorphisms and Carnosine Therapy in GWI
	Treatment; Symptoms;	DoD-171	Q10 for Gulf War Veterans
	Treatment; Symptoms;	VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic
	Treatment; Symptoms;	VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project
	Diagnosis; Symptoms;	VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome
	Treatment; Symptoms;	VA-137	Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans
Brain and Nervous System Function	Symptoms	DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms
Brain and Nervous System Function	Symptoms	DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans
Brain and Nervous System Function	Symptoms	DoD-058	Illness Among Persian Gulf War Veterans: Case Validation Studies
Brain and Nervous System Function	Symptoms	DoD-085	CNS Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms
Brain and Nervous System Function	Symptoms	DoD-101	Mechanisms in Chronic Multisymptom Illnesses
Brain and Nervous System Function	Symptoms	VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans
Brain and Nervous System Function	Symptoms	VA-071	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome
Brain and Nervous System Function	Symptoms	VA-073	Pain Sensitivity in Gulf War Veterans with Medically Unexplained Musculoskeletal Pain
Brain and Nervous System Function	Symptoms	VA-082	Pituitary Adrenal Function in People with Fatiguing Illness
Brain and Nervous System Function	Symptoms	VA-096	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain
Brain and Nervous System Function	Symptoms	VA-107	Evaluation of Stress Response Systems in Gulf War Veterans with CMI

Symptoms and General Health

Clinical

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function	Symptoms	VA-134	Autonomic Functions of Gulf War Veterans with Unexplained Illnesses
Brain and Nervous System Function	Symptoms	VA-135	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue
Brain and Nervous System Function	Diagnosis; Symptoms;	DoD-111	Autonomic Dysfunction in Gulf War Veterans
Brain and Nervous System Function	Treatment; Symptoms;	DoD-115	A Randomized, Multi-Center, Controlled Trial of Multi- Modal Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)
Brain and Nervous System Function	Treatment; Symptoms;	DoD-173	A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in Gulf War Veterans with Chronic Multisymptom Illness
Brain and Nervous System Function	Treatment; Symptoms;	VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans
Brain and Nervous System Function	Treatment; Symptoms;	VA-059	Demonstration Treatment Program for Gulf War Veterans with Unexplained Physical Symptoms
Brain and Nervous System Function	Treatment; Symptoms;	VA-062	A Randomized, Multi-Center, Controlled Trial of Multi-Modal Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V)
Brain and Nervous System Function	Treatment; Symptoms;	VA-108	Telemedicine Treatment for Veterans with Gulf War Illness
Brain and Nervous System Function;	Diagnosis; Symptoms;	DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome
Environmental Toxicology	Treatment	DoD-177	Randomized Trial of an Environmental Medicine Approach to Gulf War Veterans' Illness

Symptoms and General Health

Development

Research Focus	Project Focus	Project	Project Title
	Treatment; Symptoms;	DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain
Brain and Nervous System Function	Diagnosis; Symptoms;	DoD-168	Developing Biomarkers for Fibromyalgia

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-001 B	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not
	Symptoms	DoD-001 E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
	Symptoms	DoD-001 F	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California Who Have Separated from Active Service: GWV vs. NDV
	Symptoms	DoD-004	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey
	Symptoms	DoD-014	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry
	Symptoms	DoD-046	Exploratory Data Analysis with the CCEP Database
	Symptoms	DoD-070	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes
	Symptoms	DoD-071	A Comparison of Post Deployment Hospitalization Between Vietnam and Gulf War Veterans
	Symptoms	DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans
	Prevention	DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy
	Symptoms	DoD-116 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB)
	Symptoms	DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents
	Diagnosis	DoD-140	US Department of Defense Surveillance for Neoplasms in Infancy
	Symptoms	DoD-148	Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families
	Symptoms	DoD-150	Validation Study of Gulf War Deployment Files

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	HHS-001	Health Assessment of Persian Gulf War Veterans from Iowa
	Prevention	HHS-009	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments
	Symptoms	HHS-011	Deployment to the Gulf War and the Subsequent Development of Cancer
	Symptoms	VA-002	National Health Survey of Persian Gulf Veterans
	Symptoms	VA-002 A	VA National Survey of Persian Gulf Veterans - Phase I
	Symptoms	VA-002 B	VA National Survey of Persian Gulf Veterans - Phase II
	Symptoms	VA-004 C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance
	Symptoms	VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder
	Symptoms	VA-063 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB)
	Symptoms	VA-070	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8
	Symptoms	VA-117	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries
	Symptoms;	DoD-073	Post-deployment Morbid Stress, Behavior and Health:
	Exposure;		Developing a Model for Predicting Morbidity, Mortality, and Other Adverse Outcomes
	Prevention; Symptoms;	DoD-108	Health Status of Current National Guard Members
	Prevention; Symptoms;	DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking
	Prevention; Treatment;	HHS-010	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline
;	Symptoms	DoD-015	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm
;	Prevention	DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans
Brain and Nervous System Function	Symptoms	DoD-039	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces
;	Symptoms;	VA-001	Mortality Follow-up Study of Persian Gulf Veterans
Brain and Nervous System Function	Symptoms	DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function	Symptoms	DoD-142	Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)
Brain and Nervous System Function	Symptoms	DoD-143	Millennium Cohort Study
Brain and Nervous System Function	Symptoms	DoD-149	Longitudinal Health Study of Gulf War Veterans
Brain and Nervous System Function	Symptoms	VA-002 C	VA National Survey of Persian Gulf Veterans - Phase III
Brain and Nervous System Function	Symptoms	VA-005 A	Health and Exposure Survey of Persian Gulf Veterans
Brain and Nervous System Function	Symptoms	VA-078	Millennium Cohort Study
Brain and Nervous System Function	Symptoms	VA-118	Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004
Brain and Nervous System Function; Reproductive Health	Symptoms	DoD-045	Air Force Women's Health Surveillance Study
Environmental Toxicology	Symptoms; Exposure;	DoD-074	Relationship of Stress Exposures to Health in Gulf War Veterans
Environmental Toxicology; Chemical Weapons	Exposure; Symptoms;	DoD-116	VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V)
Environmental Toxicology; Chemical Weapons	Exposure; Symptoms;	VA-063	VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D)
Other Topics		VA-148	Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation
Reproductive Health	Symptoms	DoD-030	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study
Reproductive Health	Symptoms; Diagnosis; Prevention	DoD-096	Deployment Health Center
Reproductive Health	Symptoms; Prevention;	DoD-001	Naval Health Study Program

Symptoms and General Health

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Symptoms	VA-130	Tissue Factor and Gulf War-Associated Chronic Coagulopathies
	Symptoms	VA-131	Neuroendocrine Regulators and Proteomics in GW Veterans with CMI
	Symptoms	VA-136	Central Mechanisms Modulating Visceral Sensitivity
Brain and Nervous System Function	Symptoms	VA-115	Autonomic System Changes Cause Intestinal Symptoms in Gulf War Veterans
Brain and Nervous System Function	Symptoms	VA-119	Patterns of Microarray Gene Expression in Gulf War Illness

Symptoms and General Health

Mechanistic

Research Focus	Project Focus	Project	Project Title
Environmental Toxicology	Exposure; Symptoms;	DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness
Immune Function	Symptoms	VA-132	Immunologic Mechanisms and Biomarkers in Gulf War Illness
Immune Function	Symptoms	VA-133	Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness

Appendix C
Project Funding

(As of September 30, 2008)

NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH FROM FY 1999-2008

General Notes

1. All entries for research funding reflect money centrally obligated to researchers (both intramural and extramural) to carry out the specific projects. These funds also cover operational costs for administration, infrastructure, etc. Each department allocates these costs in slightly different ways, making it difficult to completely account for these funds. For example, in VA the research appropriation does not pay for clinician/investigator salaries. By law those funds must come from the patient care appropriation. These salary costs are not included in the obligated costs listed in the table.
2. A "blank" funding entry generally reflects years in which a project was not active (e.g., it had not started or it had come to an end).
3. Some multiyear projects receive all of their funding in the fiscal year of the authorization and appropriation. For those, the dollars authorized and obligated are shown for that fiscal year. The remaining funding entries show $0 for the years that the project is active.
4. Although all projects funded from FY 1992-2008 are listed, only the financial data for FY 1999-2008 (a 10-year window) are shown in Appendix C; Totals for FY '99-'08 do not include funds obligated in FY 1992-1998. Projects that received all of their obligated funds prior to FY 1999 will, therefore, appear in the table as having no funding. .
5. Some intramural projects/programs are supported out of operational costs. For those projects, $0 is entered for the funds in the fiscal years that the project is active.
6. Programs consisting of multiple projects are represented in one of two ways depending on how funds are centrally obligated:
   a**. Funds centrally obligated to the program**: These programs are shown in the table as a main program indicated by project designation such as DoD-1, and projects within the program as DoD-1A, DoD-1B, etc. All funds are shown under the main program. Blank funding entries are shown for the individual projects.
   b. **Funds centrally obligated to projects within a program**: The funds for these programs are only indicated by their projects without a main program identifier, for example, VA-2A and VA-2B.

Specific Notes

1. DoD-4 is part of a larger US Army study conducted at Walter Reed Army Institute of Research. Funding for this project has been combined into project DoD-23. In addition, projects DoD-8A and 8B are part of a larger US Army study in which all funding has been combined and is shown under program DoD-8.
2. HHS-3 was funded from the FY'91 appropriation, which is not included in this accounting.
3. HHS-4 was funded from the FY'93 appropriation, which is not included in this accounting.
4. Funds for VA-1 for FY'94 through FY'97 represent an aggregate of funds for both the VA Mortality Study and the VA National Survey of Persian Gulf Veterans. Beginning in FY'98, VA-1 reflects continuation of the VA Mortality Study. Beginning in FY'98, VA–2A, 2B, and 2C reflect funding for separate components of the VA National Survey of Persian Gulf Veterans.
5. In nine instances (DoD-115 & VA-062, DoD-116 & VA-063, DoD-116A & VA-063A, DoD-116B & VA-063B, DoD-118 & VA-061, DoD-119 &VA-055, DoD-125 & VA-074, DoD-143 & VA-078 ,and DoD154 & VA-88), two different designations represent the same project because both DoD and VA funded them jointly. The total funding appropriated for each of these nine projects is broken down and reported separately by funding agency.

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-001	Naval Health Study Program	C											$0
DoD-001 A	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees	C											$0
DoD-001 B	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not.	C											$0
DoD-001 C	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among Gulf War Veterans and other active-duty personnel	C											$0
DoD-001 D	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans	C											$0
DoD-001 E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study	C											$0
DoD-001 F	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV	C											$0
DoD-001 G	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War Veterans	C											$0

*Totals for FY '98 -'07 do not include funds obligated in FY 1992 -1997

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-002	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET	C											$0
DoD-004	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey	C											$0
DoD-007 A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling	C											$0
DoD-007 B	Carcinogenicity of Depleted Uranium Fragments	C	$121,400	$0									$121,400
DoD-008	Program DoD-8.	C	$0										$0
DoD-008 A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL)	C											$0
DoD-008 B	Development of a Leishmania Skin Test Antigen (LSTA)	C											$0
DoD-009	Identification of the Genetic Factors Which Control Tropism in Leishmania	C											$0
DoD-010	Pyridostigmine Synergistic Toxicity Study	C											$0
DoD-011	Male/Female Differential Tolerances to Pyridostigmine Bromide	C											$0
DoD-013	Effects of Persian Gulf War Service on Military Working Dogs	C	$200,000	$0	$0	$0	$0						$200,000
DoD-014	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry	C											$0
DoD-015	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm	C											$0
DoD-016	Kuwait Oil Fire Health Risk Assessment	C											$0
DoD-017	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning	C											$0
DoD-018	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)	C	$295,000	$295,000	$306,000	$195,000	$225,000						$1,316,000
DoD-019	Persian Gulf Veterans Health Tracking System	C	$450,000	$0	$0	$100,000	$50,000						$600,000

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-021	Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm	C											$0
DoD-022	Chronic Organophosphorus Exposure and Cognition	C	$0	$0									$0
DoD-023	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families	C											$0
DoD-030	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study	C	$0	$0	$0								$0
DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome	C	$0	$0									$0
DoD-032	Neuropsychological Functioning in Persian Gulf Era Veterans	C	$0										$0
DoD-033	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity	C	$0										$0
DoD-034	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents	C	$0										$0
DoD-035	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.	C	$10,500	$0	$0								$10,500
DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms	C	$0										$0
DoD-037	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats	C	$0										$0
DoD-038	Diagnostic Antigens of Leishmania tropica	C											$0
DoD-039	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces	C	$0	$124,868	$0								$124,868
DoD-040	Psychological and Neurobiological Consequences of the Gulf War Experience	C	$0	$0	$0								$0
DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans	C	$0	$0									$0

*Totals for FY '98 -'07 do not include funds obligated in FY 1992 -1997

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment	C	$0	$0	$0								$0
DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions	C	$14,200										$14,200
DoD-045	Air Force Women's Health Surveillance Study	C	$20,505	$0	$99,628	$0							$120,133
DoD-046	Exploratory Data Analysis with the CCEP Database	C											$0
DoD-047	Study of Mycoplasmal Infections in Gulf War Veterans	C											$0
DoD-048	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs Selected Control Groups	C											$0
DoD-049	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts	C	$0	$0									$0
DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways	C	$0										$0
DoD-051	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses	C	$0	$0									$0
DoD-052	Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans	C											$0
DoD-053	Long-Term Effects of Subclinical Exposures to Sarin	C	$0	$217,137	$0								$217,137
DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure	C	$0	$0									$0
DoD-055	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects	C	$0	$0	$0								$0

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine	C	$0	$0	$0								$0
DoD-057	Physiologic Effects of Stress in Gulf War Veterans	C	$0	$0	$0	$0							$0
DoD-058	Illness Among Persian Gulf War Veterans: Case Validation Studies	C	$0	$4,264	$267,337	$0	$0	$0					$271,601
DoD-059	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis	C	$0	$0	$0								$0
DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness	C	$0										$0
DoD-061	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid	C	$0	$0									$0
DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice	C	$0										$0
DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity	C	$0	$0									$0
DoD-064	Individual Differences in Neurobehavioral Effects of Pyridostigmine	C	$0	$190,595	$0								$190,595
DoD-065	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment	C	$0	$0	$0								$0
DoD-066	Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction	C	$403,000	$140,319	$0								$543,319
DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria	C	$0										$0
DoD-069	Five Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents	C	$0	$110,000	$0	$245,910	$0	$0	$0	$0			$355,910
DoD-070	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes	C	$115,000	$0	$0								$115,000

*Totals for FY '98 -'07 do not include funds obligated in FY 1992 -1997

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-071	A Comparison of Post Deployment Hospitalization Between Vietnam and Gulf War Veterans	C	$0	$0									$0
DoD-072	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals	C	$0	$0	$0	$0							$0
DoD-073	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes	C	$0	$0	$0								$0
DoD-074	Relationship of Stress Exposures to Health in Gulf War Veterans	C	$0	$0	$0	$0							$0
DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides	C	$0	$0	$0	$0	$0						$0
DoD-076	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel	C	$0	$0	$0	$0	$0						$0
DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War	C	$0	$0	$0	$0							$0
DoD-078	Experimental Models of Gulf War Syndrome	C	$444,800	$0	$0	$0							$444,800
DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier	C	$0	$0									$0
DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells	C	$0	$0	$0	$0							$0
DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress	C	$0	$0	$0	$0							$0
DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs	C	$0	$0	$0	$0							$0
DoD-083	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism	C	$0	$0	$0	$0							$0
DoD-084	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD	C	$0	$0	$0	$0							$0
DoD-085	CNS Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms	C	$0	$0	$0	$0							$0
DoD-086	Effects of Combat Stress on Structure and Function of the Hippocampus	C	$0	$0	$0	$0	$0						$0

*Totals for FY '98 -'07 do not include funds obligated in FY 1992 -1997

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-087	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs	C	$0	$0	$68,044	$0	$0						$68,044
DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD	C	$0	$0	$0	$0							$0
DoD-089	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder	C	$0	$0	$0	$0							$0
DoD-090	SPECT Benzodiazepine Receptor and MR Imaging in PTSD	C	$0	$0	$0	$0							$0
DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors	C	$0	$0	$0								$0
DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder	C	$0	$0	$0	$0							$0
DoD-093	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up	C	$970,700	$0	$0								$970,700
DoD-094	Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. Gulf War Veterans	C	$557,173	$206,727	$0	$0							$763,900
DoD-095	Development of Diagnostic tools and alternative treatment drugs for Leishmania	C	$1,500,000	$1,500,000	$1,500,000	$1,500,000							$6,000,000
DoD-096	Deployment Health Center	C	$1,500,000	$1,500,000	$2,250,000	$1,750,000	$1,750,000	$1,750,000	$0				$10,500,000
DoD-097	Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis	C	$177,300	$146,742	$151,202	$151,000							$626,244
DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans	O	$332,500	$188,000	$364,182	$0	$0	$0	$0	$0	$0	$0	$884,682

*Totals for FY '98 -'07 do not include funds obligated in FY 1992 -1997

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-099	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations	C	$207,876	$204,205	$224,265	$0	$0						$636,346
DoD-100	Antibodies to Squalene	O	$582,756	$0	$50,000	$487,333	$0	$0	$0	$0	$0	$0	$1,120,089
DoD-101	Mechanisms in Chronic Multisymptom Illnesses	O	$2,903,408	$5,542,189	$0	$4,786,192	$644,870	$4,781,952	$2,429,999	$0	$0	$0	$21,088,610
DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans	C	$249,908	$0	$253,793	$0	$281,950						$785,651
DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals	O	$583,319	$46,315	$0	$0	$349,994	$242,424	$160,000	$326,570	$166,570	$0	$1,875,192
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome	C	$1,003,937	$9,311	$0	$0	$40,844						$1,054,092
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala	C	$950,490	$0	$0	$0	$0	$0					$950,490
DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness	C	$292,411	$0	$0	$0							$292,411
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity	C	$875,373	$10,825	$0	$0	$0	$0					$886,198
DoD-108	Health Status of Current National Guard Members	C	$578,970	$0	$264,375	$174,651	$0	$0	$0				$1,017,996
DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms	C	$917,762	$147,523	$397,243	$0	$0						$1,462,528
DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy	C	$127,920	$63,705	$0	$0							$191,625
DoD-111	Autonomic Dysfunction in Gulf War Veterans	C	$999,144	$0	$0	$0	$189,609	$0	$0				$1,188,753
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	C	$256,916	$0	$0	$0							$256,916
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects	C	$802,140	$0	$0	$0	$0	$0					$802,140
DoD-114	A Re-examination of Neuropsychological Functioning in Persian Gulf War Veterans	C	$593,712	$0	$0	$0							$593,712

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-115	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)	C	$1,000,000	$2,000,000	$0	$0							$3,000,000
DoD-116	VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V)	C	$250,000	$250,000	$250,000	$250,000	$250,000						$1,250,000
DoD-116 A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA)	C											$0
DoD-116 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB)	C											$0
DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking	C		$1,232,050	$0	$0							$1,232,050
DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also VA-61)	C		$430,824	$832,272	$0							$1,263,096
DoD-119	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also VA-55)	C	$500,000	$1,000,000	$0	$0							$1,500,000
DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents	C	$239,000	$316,000	$0	$0							$555,000
DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development	C	$25,000	$15,000	$15,000								$55,000
DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys	C	$25,000	$30,000	$35,000								$90,000
DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys	C	$15,000	$20,000	$15,000								$50,000
DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin	C	$1,283,218	$0	$0	$0	$0	$0	$0				$1,283,218
DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74)	C		$445,078	$0	$0	$0	$0	$0				$445,078

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-126	Blood-Brain Barrier Transport of Uranium	O		$790,884	$0	$0	$0	$0	$0	$0	$0	$0	$790,884
DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man	C			$399,582	$0	$0						$399,582
DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity	O		$661,156	$0	$0	$328,734	$0	$89,055	$0	$0	$0	$1,078,945
DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness	O			$1,276,220	$0	$0	$0	$0	$0	$0	$0	$1,276,220
DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents	O			$983,164	$0	$0	$0	$0	$0	$0	$0	$983,164
DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses	O			$5,377,526	$0	$500,000	$0	$0	$0	$0	$0	$5,877,526
DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness	C			$792,198	$0	$0	$0	$0	$0			$792,198
DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome	C			$884,087	$0	$0	$0	$0	$0			$884,087
DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin	O		$775,155	$0	$0	$0	$0	$0	$0	$0	$0	$775,155
DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorous Exposure	C		$786,408	$0	$0	$0	$0	$0				$786,408
DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure	C			$748,858	$0	$0	$0	$0				$748,858
DoD-137	Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin	C			$600,111	$0	$0	$0	$0	$0			$600,111
DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents	O			$434,795	$0	$0	$0	$0	$0	$0	$0	$434,795

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses	C		$892,399	$500,885	$0	$0						$1,393,284
DoD-140	US Department of Defense Surveillance for Neoplasms in Infancy	C			$764,879	$0	$0	$0	$0	$0			$764,879
DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans	C			$149,993	$0	$0						$149,993
DoD-142	Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)	C					$168,962	$0		$0			$168,962
DoD-143	Millennium Cohort Study	O		$3,000,000	$1,000,000	$1,250,000	$2,000,000	$1,950,000	$2,880,000	$2,893,000	$3,251,000	$3,160,000	$21,384,000
DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces	O	$109,000	$295,000	$250,000	$300,000		$0	$0	$0	$0	$0	$954,000
DoD-145	Early Intervention Research Program to Enhance Soldier Resilience	O			$250,000	$275,000	$275,000	$0	$0	$0	$0	$0	$800,000
DoD-146	Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War	C			$100,000								$100,000
DoD-147	Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications	C	$190,000	$260,000	$412,000	$696,111	$292,530	$0	$0	$0			$1,850,641
DoD-148	Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families	C			$100,000								$100,000
DoD-149	Longitudinal Health Study of Gulf War Veterans	C			$1,689,945	$0	$0	$0	$0	$0			$1,689,945
DoD-150	Validation Study of Gulf War Deployment Files	C				$134,348	$0						$134,348
DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War Veterans	C				$482,274	$0	$0	$0	$0			$482,274
DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents	O				$1,000,000	$1,019,440	$0	$0	$0	$0	$0	$2,019,440
DoD-153	Gulf War Illness Research	C			$4,694,500	$4,950,000	$920,838	$2,003,000	$928,000	$0			$13,496,338
DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study	O				$100,000	$566,542	$368,687	$604,372	$0	$0	$0	$1,639,601

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide	O					$1,021,862	$0	$0	$0	$0	$0	$1,021,862
DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant	O					$1,519,951	$0	$0	$0	$0	$0	$1,519,951
DoD-157	Novel Leishmania And Malaria Potassium Channels: Candidate Therapeutic Targets	C			$789,805	$0	$0	$0	$0				$789,805
DoD-158	Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission Of Genetic Damage To Offspring	C			$382,829	$0	$0	$0	$0	$0			$382,829
DoD-159	Neurotoxicity from Chronic Exposure to Depleted Uranium	C			$965,931	$0	$0	$0	$0	$0			$965,931
DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium	C			$696,357	$0	$0	$0	$0				$696,357
DoD-161	Glutamate Receptor Aptamers and ALS	O					$1,152,744	$0	$0	$0	$0	$0	$1,152,744
DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function	O					$1,041,751	$0	$0	$0	$0	$0	$1,041,751
DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin	O					$1,828,876	$0	$0	$0	$0	$0	$1,828,876
DoD-164	Efficacy of Adjunct Sleep Interventions For PTSD (EASI-PTSD)	O							$999,623	$0	$0	$0	$999,623
DoD-165	Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military - BALSAM	O							$1,000,799	$0	$0	$0	$1,000,799
DoD-166	A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance	O							$1,000,000	$0	$0	$0	$1,000,000
DoD-167	Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure	O								$637,848	$0	$0	$637,848
DoD-168	Developing Biomarkers for Fibromyalgia	O								$936,067	$0	$0	$936,067
DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain	O								$840,574	$0	$0	$840,574

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I	O								$208,353	$0	$0	$208,353
DoD-171	Q10 for Gulf War Veterans	O								$718,261	$0	$0	$718,261
DoD-172	CNDP1 Polymorphisms and Carnosine Therapy in GWI	O								$831,200	$0	$0	$831,200
DoD-173	A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in Gulf War Veterans with Chronic Multisymptom Illness	O								$650,279	$0	$0	$650,279
DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness	O								$687,530	$0	$0	$687,530
DoD-175	Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium	O								$767,061	$0	$0	$767,061
DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome	O								$112,500	$0	$0	$112,500
DoD-177	Randomized Trial of an Environmental Medicine Approach to Gulf War Veterans' Illness	O								$445,865	$0	$0	$445,865
DoD-178	Analysis of Paraoxonase Status among US Navy Gulf War Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions	O								$73,153	$0	$0	$73,153
	TOTAL DOD FUNDS		$22,674,338	$23,847,679	$31,587,006	$18,827,819	$16,419,497	$11,096,063	$10,091,848	$10,128,261	$3,417,570	$3,160,000	$151,250,081

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Department of Health and Human Services Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
HHS-001	Health Assessment of Persian Gulf War Veterans from Iowa	C	$162,000	$0	$0								$162,000
HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18	C	$0	$0									$0
HHS-003	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires	C											$0
HHS-004	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian Gulf War Veterans In Mississippi	C											$0
HHS-005	Cognitive Function and Symptom Patterns in Persian Gulf Veterans	C	$558,000	$660,000	$0	$0							$1,218,000
HHS-006	Defining Gulf War Illness	C	$480,000	$719,792	$200,000	$0							$1,399,792
HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid	C	$192,445	$187,647	$0								$380,092
HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures	C	$247,933	$0	$0								$247,933
HHS-009	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments	C			$337,693	$339,814	$339,814	$0	$0	$0	$0		$1,017,321
HHS-010	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline	C			$461,177	$460,000	$460,000	$0	$0	$0	$0		$1,381,177
HHS-011	Deployment to the Gulf War and the Subsequent Development of Cancer	C					$164,291	$0	$0	$0	$0		$164,291
HHS-012	Genetic Epidemiology of ALS in Veterans	O						$466,126	$466,481	$455,587	$441,974	$433,467	$2,263,635
	TOTAL HHS FUNDS		$1,640,378	$1,567,439	$998,870	$799,814	$964,105	$466,126	$466,481	$455,587	$441,974	$433,467	$8,234,241

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Status: C=Complete; O=Ongoing

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-001	Mortality Follow-up Study of Persian Gulf Veterans	C	$166,848	$176,440	$171,154	$128,496	$0						$642,938
VA-002	National Health Survey of Persian Gulf Veterans	C	$0	$0	$0	$0							$0
VA-002 A	VA National Survey of Persian Gulf Veterans - Phase I	C											$0
VA-002 B	VA National Survey of Persian Gulf Veterans - Phase II	C	$0										$0
VA-002 C	VA National Survey of Persian Gulf Veterans - Phase III	C	$3,571,932	$3,400,000	$2,344,427	$30,000							$9,346,359
VA-003	Use of Roster of Veterans Who Served in Persian Gulf Area	C	$0										$0
VA-004	Boston Environmental Hazards Research Center Program	C	$500,000	$229,500									$729,500
VA-004 A	Evaluation of Cognitive Functioning of Persian Gulf Veterans	C											$0
VA-004 B	Evaluation of Neurological Functioning in Persian Gulf Veterans	C											$0
VA-004 C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance	C											$0
VA-004 D	Evaluation of Respiratory Dysfunction Among Gulf War Veterans	C											$0
VA-004 E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility	C											$0
VA-004 F	Validity of Computerized Tests	C											$0
VA-005	East Orange Environmental Hazards Research Center Program	C	$500,000	$326,900									$826,900
VA-005 A	Health and Exposure Survey of Persian Gulf Veterans	C											$0
VA-005 B	Physiological and Psychological Assessments of Persian Gulf Veterans	C											$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-005 C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans	C											$0
VA-005 D	Effects of Genetics and Stress on Responses to Environmental Toxins	C											$0
VA-006	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research	C	$499,098	$233,290									$732,388
VA-006 A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)	C											$0
VA-006 B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)	C											$0
VA-006 C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)	C											$0
VA-006 D	DNA Damage from Chemical Agents and Its Repair (Project IV)	C											$0
VA-006 E	Clinical and Epidemiology Leishmania Research	C											$0
VA-007	Desert Storm Reunion Survey	C											$0
VA-008	Psychological Test Data of Gulf War Veterans Over Time	C	$0	$0	$0	$0							$0
VA-009	Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems	C											$0
VA-010	Memory and Attention in PTSD	C	$0										$0
VA-011	Neuropsychological Functioning in Veterans	C											$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-012	Psychological Assessment of Operation Desert Storm Returnees	C											$0
VA-013	Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study	C											$0
VA-015	Vaccine-Mediated Immunity Against Leishmaniasis	C	$79,400	$41,540	$114,336	$119,600	$59,800						$414,676
VA-016	Protective Immunity in Experimental Visceral Leishmaniasis	C											$0
VA-017	Immunological Evaluation of Persian Gulf Veterans	C											$0
VA-018	Chronic Gastrointestinal Illness in Persian Gulf Veterans	C											$0
VA-020	Psychological Adjustment in Operation Desert Shield/Storm Veterans	C											$0
VA-021	A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS	C											$0
VA-036	Stress Symptoms and Their Causal Attribution in Desert Storm Veterans	C											$0
VA-040	Musculoskeletal Symptoms in Gulf War Syndrome	C	$0										$0
VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder	C	$0	$0									$0
VA-047	Retrospective Verification of Mustard Gas Exposure	C	$299,700	$139,960									$439,660
VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance	C	$89,400	$92,840	$45,000								$227,240
VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction	C	$147,950	$141,696	$144,024	$125,862							$559,532
VA-050	Neuropsychological findings in a sample of Operation Desert Storm Veterans	C											$0
VA-051	Psychobiological Assessment of Desert Storm Veterans	C	$0	$0	$0								$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-053	Spouses and Children Program	C	$51,088	$33,655	$12,934	$25,000							$122,677
VA-054	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress	C	$53,400	$90,131	$86,895	$86,350	$72,700	$39,375					$428,851
VA-055	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)	C	$447,742	$1,466,375	$1,981,963	$254,000							$4,150,080
VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)	C	$261,625	$161,175									$422,800
VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)	C	$253,625	$174,750									$428,375
VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)	C	$349,805	$262,496									$612,301
VA-059	Demonstration Treatment Program for Gulf War Veterans With Unexplained Physical Symptoms (13)	C	$348,225	$259,500									$607,725
VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans	C	$328,500	$246,375									$574,875
VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also DoD-118)	C		$0	$0	$110,600							$110,600
VA-062	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V)	C	$788,000	$3,756,826	$1,971,233	$44,250							$6,560,309
VA-063	VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D)	C	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000		$2,250,000

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-063 A	Follow-Up Investigation of troops exposed to nerve agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA)	C											$0
VA-063 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB)	C	$0										$0
VA-064	Boston Environmental Hazards Research Center	C		$112,360	$299,700	$300,000	$297,000	$337,200	$337,200	$337,200			$2,020,660
VA-064 A	Functional Neuroimaging in Lead Exposed Adults	C											$0
VA-064 B	Quantification and Validation of Structure-Function relationships through visuospatial test performance	C											$0
VA-064 C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in Veteran populations	C											$0
VA-065	San Antonio Environmental Hazards Research Center	C		$116,750	$350,000	$300,000	$300,000	$337,200					$1,403,950
VA-065 A	Does a variant of the human SOD2 gene increase sensitivity to hazards?	C											$0
VA-065 B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress	C											$0
VA-065 C	The importance of hydrogen peroxide detoxification in cellular protection	C											$0
VA-065 Cont'	San Antonio Environmental Hazards Research Center	C											$0
VA-065 D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards?	C											$0
VA-066	Physiological Responding in Posttraumatic Stress Disorder	C	$0	$0	$0								$0
VA-067	Olfactory Functioning in Gulf War Veterans	C		$7,500	$7,500								$15,000

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-068	Family Study of Fibromyalgia	C		$46,700	$50,000	$50,000							$146,700
VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans	C		$122,243	$135,487	$141,815	$48,947						$448,492
VA-070	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8	C	$19,817	$6,204	$4,884	$4,900							$35,805
VA-071	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome	C		$125,313	$181,692	$186,524	$47,975						$541,504
VA-072	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses	C				$50,000	$50,000						$100,000
VA-073	Pain Sensitivity in Gulf War Veterans with Medically Unexplained Musculoskeletal Pain	C				$50,000	$50,000						$100,000
VA-074	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)	C			$291,804	$896,550	$1,346,863	$1,912,448					$4,447,665
VA-075	ALS and Veterans: Are Veterans at Increased Risk?	C			$73,000	$139,600	$139,600	$78,455					$430,655
VA-076	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD	C				$145,100	$135,000	$151,740					$431,840
VA-077	HPA Axis Reactivity in Men and Women with Chronic PTSD	C				$101,400	$101,300	$113,861					$316,561
VA-078	Millennium Cohort Study	O											$0
VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress	O					$203,400	$119,818	$248,458	$253,277	$252,602		$1,077,555
VA-081	Stress, Pro-Inflammatory Cytokines and Coping Behavior	C					$193,800	$186,035					$379,835
VA-082	Pituitary Adrenal Function in People with Fatiguing Illness	C				$88,000	$135,000	$151,740	$276,112	$121,842			$772,694

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-083	Neuropsychological Assessment of a Population-Based Sample of Persian Gulf War Veterans and Controls	C				$18,988	$50,000	$31,012					$100,000
VA-084	Neurobiology of Severe Psychological Trauma in Women	C				$135,000	$135,000	$151,740					$421,740
VA-085	Associative Learning in Veterans with and without Combat Experience	C				$60,400	$74,000	$232,458					$366,858
VA-086	A Clinical Trial of Magnetic Stimulation in Depression	C				$131,400	$131,400	$147,694					$410,494
VA-087	Improving Outcomes of Depression in Primary Care	C				$152,065	$201,926	$218,280					$572,271
VA-088	Prospective Assestment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study	C					$24,057	$47,011					$71,068
VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis	C					$319,229	$625,564	$799,104	$863,951			$2,607,848
VA-090	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness	C					$250,000	$281,000	$281,000	$449,990	$449,990		$1,711,980
VA-090A	Neuronal Hyperexcitability and Motor Neuron Regeneration	C											$0
VA-090B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders	C											$0
VA-090C	Developmental Differences in Alcohol Withdrawal Sensitivity	C											$0
VA-090D	Seizures and Neuroplasticity:Physiology and Biochemistry	C											$0
VA-091	The Role of Dietary Choline in Neuroprotection	C						$196,951					$196,951
VA-092	Acetylcholinesterase Activity In Gulf War Veterans	C					$89,920	$49,833					$139,753

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-093	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans	C					$56,750	$36,080	$163,205	$127,405			$383,440
VA-094	The Immunology of Chronic Cutaneous Leishmaniasis	C						$192,204	$157,360	$202,320			$551,884
VA-095	The Role of Signal Regulatory Proteins in Astrocytomas	C					$54,158	$231,566	$238,239	$178,679			$702,642
VA-096	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain	O						$49,035	$128,698	$70,302	$135,127	$95,382	$478,544
VA-097	Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas	C					$99,563	$215,093	$241,957	$246,355	$134,628		$937,596
VA-098	Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas	C						$44,420	$168,600	$168,600			$381,620
VA-099	Vaccination Against Visceral Leishmaniasis with a multi-epitope vaccine	C				$65,700	$123,413	$116,896	$118,863	$117,908			$542,780
VA-100	Studies of the Blood-Brain Barrier and its Manipulation	C				$151,875	$151,875	$151,740	$151,740	$151,740			$758,970
VA-101	Biomarkers Discovery in ALS	O						$50,518	$227,130	$151,555	$112,009	$299,165	$840,377
VA-102	Cholinergic and Monoaminergic Influences on Sleep	C			$60,642	$92,588	$92,588	$134,160	$175,814	$134,328			$690,120
VA-103	Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal	C					$210,600	$296,657	$307,253	$317,845			$1,132,355
VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome	C					$114,975	$168,600	$168,600	$84,300			$536,475
VA-105	Expression of the Major Surface Protease of Leishmania Chagasi	C				$76,613	$135,628	$298,175	$119,535	$92,817			$722,768
VA-106	Interoceptive Stressor Conditioning: A Model for Gulf War Illness	C							$193,440	$198,161			$391,601
VA-107	Evaluation of Stress Response Systems in Gulf War Veterans with CMI	O							$192,766	$117,412	$210,637	$173,321	$694,136
VA-108	Telemedicine Treatment for Veterans with Gulf War Illness	O							$185,714	$238,616	$224,916	$11,100	$660,346

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-109	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics	O							$158,372	$306,912	$317,503	$321,148	$1,103,935
VA-110	Pain Among Gulf War Veterans: Secondary Analysis of CSP#458 Data	C							$96,439	$48,557			$144,996
VA-111	T Cell Responses to Multiple Immunizations and Stress	C							$112,399	$112,399			$224,798
VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium	C							$1,171,208	$734,590			$1,905,798
VA-113	Novel Cause of Motor Neuron Disease	O							$166,352	$110,152	$110,152	$ 110,152	$496,808
VA-114	Strategies in Therapeutic Development of Neurodegenerative Diseases	C							$266,950	$370,920			$637,870
VA-115	Autonomic System Changes Cause Intestinal Symptoms in Gulf War Veterans	C							$275,623	$275,623			$551,246
VA-116	Quantitative Trait Genes Controlling Circadian and Sleep Behaviors	C							$125,888	$228,734			$354,622
VA-117	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries	O							$42,206	$151,740	$115,772	$66,597	$376,315
VA-118	Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004	C							$42,262	$160,535	$119,453		$322,250
VA-119	Patterns of Microarray Gene Expression in Gulf War Illness	C							$192,204	$168,600	$168,600		$529,404
VA-120	Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis	C							$90,988	$165,116			$256,104
VA-121	Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders	C							$295,938	$441,612			$737,550
VA-122	Role of Mitochondrial Oxidative Stress in ALS	C							$55,188	$271,896			$327,084
VA-123	Interactions Between Maternal Care, Stress and Pyridostigmine Bromide	C							$60,134	$48,332	$178,447		$286,913

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PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-124	Early Life Determinants of Vulnerability to Pyridostigmine Bromide	C							$213,110	$195,688			$408,798
VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla	O							$322,532	$479,892	$743,778	$653,747	$2,199,949
VA-126	Structural Magnetic Resonance Imaging in Gulf War-Era Veterans	C							$159,552	$165,565	$165,565		$490,682
VA-127	Interactions of the Leishmania sp. with Mammalian Cells	C							$101,216	$166,464			$267,680
VA-128	MR Tracking of Stem Cells for Replacement Therapy in ALS	C							$236,730	$236,730			$473,460
VA-129	Glucocorticoid Responsivity in Gulf War Veterans	C							$168,600	$167,164	$168,600		$504,364
VA-130	Tissue Factor and Gulf War-Associated Chronic Coagulopathies	O								$194,826	$217,055	$248,741	$660,622
VA-131	Neuroendocrine Regulators and Proteomics in GW Veterans with CMI	C								$60,767	$163,579		$224,346
VA-132	Immunologic Mechanisms and Biomarkers in Gulf War Illness	O								$64,630	$112,400	$112,400	$289,430
VA-133	Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness	C								$112,400	$112,400		$224,800
VA-134	Autonomic Functions of Gulf War Veterans with Unexplained Illnesses	O								$8,880		$0	$8,880
VA-135	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue	O								$6,744		$0	$6,744
VA-136	Central Mechanisms Modulating Visceral Sensitivity	C								$83,288			$83,288
VA-137	Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans	O								$161,968	$224,294	$217,325	$603,587

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Status: C=Complete; O=Ongoing

PROJECT NO	PROJECT TITLE	STATUS	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	TOTALS FY 99-08
VA-138	Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP	O								$226,773	$235,240	$258,136	$720,149
VA-139	Sleep Neurobiology and Circuitry	C								$33,720			$33,720
VA-140	Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS	C								$232,553			$232,553
VA-141	Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis	C								$243,779			$243,779
VA-142	VA Gulf War Biorepository Trust	O								$991,510	$991,510	$1,091,547	$3,074,567
VA-143	The Role of Protein Oxidation in the Progression of ALS	C								$112,400	$112,400		$224,800
VA-144	Testing the Role of Permethrin on the Progression of ALS	C								$112,400	$112,400		$224,800
VA-145	Proteomic Analysis of Cellular Response to Biological Warfare Agents	O								$129,260	$224,800	$224,800	$578,860
VA-146	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route	O								$161,687	$256,159	$245,295	$663,141
VA-147	The Diagnosis and Pathogenesis of Occult Leishmaniasis	C								$98,350			$98,350
VA-148	Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation	C								$24,307	$71,008		$95,315
VA-149	Behavior of Neural Stem Cells in a Rat Model of GWS	O									$129,861	$268,901	$398,762
VA-150	Gulf War Veterans Illnesses' Research IDIQ Contract	O									$15,000,000	$15,000,000	$30,000,000
VA-151	Genetic Epidemiology of ALS	O										$ 2,116,602	$ 2,116,602
VA-152	Multiple Sclerosis in Gulf War Veterans	O										$122,010	$122,010
	TOTAL VA FUNDS		$9,006,155	$12,020,519	$8,576,675	$4,512,676	$5,746,467	$7,644,559	$9,484,679	$12,942,066	$21,977,767	$21,636,369	$113,391,050

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