Department of Veterans Affairs

ANNUAL REPORT TO CONGRESS

Federally Sponsored Research on Gulf War Veterans' Illnesses for 2009

August 2010

Deployment Health Working Group Research Subcommittee

Annual Report to Congress – 2009

Federally Sponsored Research on Gulf War Veterans' Illnesses for 2009

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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 and section 502 of Public Law 111-163, 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 *2009 Annual Report to Congress*, which is the sixteenth 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) 2000 through FY 2009; 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 2009

Section III provides brief summaries of research articles on the health problems of GW Veterans published during calendar year 2009 or in 2008 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 2009 the Department of Veterans Affairs (VA), Department of Defense (DoD), and Department of Health and Human Services (HHS) funded 361 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 $267 million for the period from FY 2000 through FY 2009. As of September 30, 2009, 295 projects (82 percent of the 361 projects) were completed, and 66 projects (18 percent) were new or ongoing.

V. NEW RESEARCH PROJECTS AND INITIATIVES

Twelve projects were funded through the FY08 appropriation for the Gulf War Illness Research Program (GWIRP) managed by the Congressionally Directed Medical Research Program (CDMRP) at DoD, but did not start until FY 2009. These projects focused on Brain and Nervous System Function (3), Environmental Toxicology (2), and Symptoms and General Health (7). VA funded 2 new projects in FY 2009 focused on Brain and Nervous System Function (1) and Symptoms and General Health (1).

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 and section 502 of Public Law 111-163, 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 2009*, which is the sixteenth report on research and research activities (DHWG, 2004; DHWG, 2005; DHWG, 2006a; DHWG, 2006b; DHWG, 2007; DHWG, 2008; DHWG, 2009; MVHCB, 2001; MVHCB, 2002; PGVCB, 1995; 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 2000 through FY 2009. 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 2009

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 64 relevant articles published in English in calendar year 2009 or in 2008 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 Persian Gulf War I Veterans are presented in this section if they are related to brain and nervous system function. In 2009, most of these studies focused on amyotrophic lateral sclerosis and neuroinflammation, although a small number of review articles, mainly focused on neuropsychological findings in this population, were also summarized here.

General Brain Function and Exposure Research

Rice and co-workers (Rice et al., 2009) examined the association between PON1 Q192R polymorphism and self-reported poor health and depression in two large population studies. Despite having been previously associated with Gulf War exposure outcomes, no association was evidence for poor general or mental health in the two independent samples. One publication (Friedl et al., 2009) provided a general assessment of the results of DoD's investment of more than $150 Million into GWI research and concluded that that no specific neurotoxic chemical exposure has explained the illnesses observed in Gulf War (GW) Veterans. Much of the investment however has provided important generalizable scientific information.

N-acetylaspartate (NAA) is considered a marker of axonal integrity expressed in a ratio to creatine. Patients received glatiramer acetate therapy and annual brain scans were conducted (Khan et al., 2008). In the first year of therapy multiple sclerosis subjects in the treatment group showed increase NAA/Cr, as did three subjects in the control group.

A review of the evidence of exposure to organophosphate and carbamate acetylcholinesterase inhibitors in GW Veterans and their relationship to reported illnesses (Golomb, 2008) suggested that many epidemiological studies report an association. Haley and co-workers (Haley et al., 2009) reported that following a challenge of physostigmine, no characterization was evident for Gulf War Veterans differentiated using their previously complex 1, 2 and 3. Since some changes were identified in subgroups, the authors concluded there may be deep brain structure dysfunction. Barbier (Barbier et al., 2009) described the consequences of repeated pyridostigmine bromide (PB) administration in rats and showed increase in three genes implicated in memory in the hippocampus, an area of the brain important for memory, and suggest that genomic changes may occur following exposure to PB.

.**Amyotrophic Lateral Sclerosis (ALS)**

One study systematically reviewed the evidence of associations between sporadic ALS and chemical/metal exposure (Sutedja et al., 2009). Of the 88 studies reviewed, 7 chemical and 3 metal exposure publications met validity criteria for the review and of these an association of pesticides to increased ALS risk was reported in two. Cox and co-workers (Cox et al., 2009) focused on inhalation of cyanotoxins carried by dues in the Gulf region as a possible inhalant exposure/ALS risk factor for GW Veterans. Another potential risk factor is aluminum hydroxide, an adjuvant in anthrax and other vaccines. Shaw and Petrik (Shaw and Petrik, 2009) examined the toxicity of aluminum hydroxide in mice and for changes in motor neurons as well as motor function impairments following injections of aluminum hydroxide. Two studies examined survival rates and features in ALS patients. Pastula and co-workers (Pastula et al., 2009) found that older age at diagnosis and past service in Vietnam were associated with shortened survival from time of diagnosed onset. Karsarskis and co-workers (Kasarskis et al., 2009) compared survival rates of deployed to non-deployed GW

Veterans with ALS. They found that the deployed group has shorter survival post onset than non-deployed (40.2 vs 57.0 months) in the absence of any other significant clinical features.

Neuropsychological Functioning and Stress Response

Toomey and co-workers (Toomey et al., 2009) studied 2189 GW era Veterans' neuropsychological functioning ten years post deployment and reported deficits in deployed Veterans on motor speed and attention, as well as some deficits on individual test variables. Self-reported exposure to toxicants was associated with impaired performance, as was depression in relation to attention. In contrast, Wallin and colleagues (Wallin et al., 2009) examined neuropsychological functioning in Gulf War Veterans who met CDC criteria and found no significant differences in performance between groups on traditional and computerized battery. Woodward and co-workers (Woodward et al., 2009b) examined cortical volume in combat related PTSD in Vietnam and Gulf War Veterans, and reported cortical volume, thickness and area were smaller; these changes they were not correlated to PTSD or intelligence (Woodward et al., 2009a). A study of Veterans with PTSD from all deployments (14 percent from the 1990-1991 Gulf War) found that Veterans with higher severity of PTSD were more likely to meet diagnostic criteria for metabolic syndrome and may be at risk for for diminished health and increased morbidity (Heppner et al., 2009). Golier and colleagues reported a study of Gulf War Veterans with PTSD and unexplained health symptoms who underwent a metyrapone stimulation test to examine cortisol changes and found PTSD symptoms and unexplained medical health symptoms were positively associated with ACTH reponse, and that deployment in general may have enduring effect on pituitary function (Golier et al., 2009). A study of repeated stress exposures combined with pyridostigmine treatment was modelled in rats, however there were no indications that pyridostigmine actually crossed the brain blood barrier, suggesting mediation of any functional deficits would have been mediated peripherally (Amourette et al., 2009). A study of Australian GW Veterans (McKenzie et al., 2009) showed that onset of new psychological disorders post-deployment to the Persian Gulf peaked in the first two years, with alcohol use disorders prominently appearing first. Another study compared physical, psychological, and functional comorbidities in Australian male Gulf War I veterans with those in actively (non-Gulf) deployed and nondeployed military personnel (Kelsall et al., 2009). Multisymptom illness was more common in male GW veterans than in the comparison group. GW veterans with multisymptom illness had increased psychiatric disorders (including major depression and posttraumatic stress disorder), increased unexplained chronic fatigue, and more reported functional impairment and poorer quality of life; objective physical and laboratory outcomes were similar, however, to those for veterans without multisymptom illness. Smith-Osborne (Smith-Osborne, 2009) examined the post-deployment attainment of higher education and reported factors that positively influence the use of educational benefits for Veterans including treatment for PTSD, small nuclear family, and higher family income.

B. Environmental Toxicology

Environmental agents potentially toxic to GW Veterans in theater were the topics of numerous scientific reports in 2009. These agents can be divided into 4 groups: (1) depleted uranium (DU), which is used in armor-piercing munitions; (2) anti-nerve agents (e.g., pyridostigmine bromide); (3) insecticides (e.g., permethrin, chlorpyrifos); and (4) insecticide repellents (e.g., DEET).

Depleted Uranium (DU)

There were a series of publications describing various parts of a large study called the Capstone Depleted Uranium (DU) Aerosol Study (Cheng et al., 2009; Daxon et al., 2009; Guilmette et al., 2009; Guilmette and Cheng, 2009; Hahn et al., 2009; Holmes et al., 2009; Krupka et al., 2009; Miller et al., 2009; Parkhurst et al., 2009; Parkhurst and Guilmette, 2009a; Parkhurst and Guilmette, 2009b; Roszell et al., 2009; Szrom et al., 2009). These publications developed an empirical basis for determining the inhalation exposure to DU aerosols and the exposure and risk to personnel in combat vehicles struck by DU containing penetrators. A different study focused on the environmental conditions that would enhance the bioavailability of soil uranium (Lind et al., 2009) while another study (Li et al., 2009) developed a model to estimate the biological radiation dose received from various sources (e.g. alimentary tract, lung) associated with the size of aerosolized DU. A long-term (i.e., 16 years to date) longitudinal surveillance studies of United States Veterans exposed to DU from friendly fire in the 1990-1991 Gulf War found that the level of urinary excretion of uranium was associated with the DU retained shrapnel burden. This continuing Baltimore Veterans Administration Medical Center study found no other significant differences during a 3-day clinical assessment (McDiarmid et al., 2009). Furthermore, No urine U measure with a "depleted" isotopic signature has been detected in U.S. veterans without a history of retained DU embedded fragments from previous injury. These findings suggest that future DU-related health harm is unlikely in Veterans without DU fragments (Dorsey et al., 2009). The biological effects of DU were examined in various isolated cell and animal models. Chronic oral exposure to low dose DU was given to rats and then to their offspring to evaluate the genotoxicity of DU (Hao et al., 2009). The offspring had stored

more uranium then the parents in kidney and ovary. The offspring also showed more abnormalities in the measured parameters than did the parents. Another study of rats chronically ingesting either DU or uranium (not radioactive) showed changes in anti-oxidant defense mechanisms in the brain of both groups although greater changes seen with DU than uranium (Lestaevel et al., 2009). This study suggests that the biological effects of DU derive both from the radio-toxicity as well as heavy metal or chemical toxicity. There were two studies looking at implanted DU in rats. One study showed that uranium deposition was higher in kidney and bone than in other tissues (Zhu et al., 2009). Another study (Arfsten et al., 2009) looked at the effects on reproduction in both parents and offsprings. There were no measured biological effects on reproduction in the parental group; however, the mature offspring showed a slight increase in gestation time. Isolated human lung cells exposed in culture to particulate DU showed increased neoplastic transformation, which was associated with chromosomal instability (Xie et al., 2009).

Nerve Agents

Rodents exposed to a combination of pyridostigmine and stress showed that repeated stress had an effect on various measures of behavior such as impulsiveness and aggression (Lamproglou et al., 2009). Rats with single and multiple low-level inhalation exposures to sarin did not exhibit overt signs of clinical toxicity but did have cognitive and performance deficits. The observed deficits did not appear to be persistent (Genovese et al., 2009).

Insecticides and Pesticides

Several studies looked at the effects of insecticides and pesticides on humans. In a well-controlled study, individuals wearing permethrin-impregnated battle dress uniform for 28 days showed elevated levels of permethrin catabolic metabolites although the absorbed permethrin was below the acceptable daily intake, which suggest that health effects would be unlikely (Rossbach et al., 2009). Vegetable farmers with chronic low-level exposure to organophosphates compared to farmers not using organophosphates showed neurological effects that might affect attention and memory (Dassanayake et al., 2009). There are several studies focusing on the cellular and intracellular effects of organophosphate pesticides. Two studies (Grigoryan et al., 2008; Grigoryan et al., 2009) showed that isolated proteins tightly bound organophosphates at tyrosine and lysine residues suggesting that organophosphates may have widespread effects on many proteins. Mice injected subcutaneously with DEET showed immunotoxicity, which could contribute to immunosuppression.

C. Immune Dysfunction and Infectious Diseases

Whistler and colleagues examined 9 patients meeting the CDC definition (Fukuda et al., 1998) for Gulf War Illness (GWI) and 11 matched sedentary controls who had not been deployed to the Persian Gulf, in a small pilot study of the effect of a standard bicycle ergometer exercise challenge on immune function measured with classic immune assays and gene expression profiling (Whistler et al., 2009). The investigators noted that GWI patients demonstrated impaired immune cell function compared to control subjects and that the exercise challenge augmented the differences. They suggesed that immune cell dysfunction may play a role in sustaining GWI.

D. Reproductive Health

No publications in 2009.

E. Symptoms and General Health

Chronic fatigue syndrome (CFS) and fibromyalgia (FM) commonly co-occur. Some propose that CFS 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, 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 long-term longitudinal study addressed numerous issues related to GW and other Veterans. A study (Barth et al., 2009) to address mortality from various neurological disorders began in 1991 when the Veterans left the GW Theater of operations and concluded in 2004. When GW Veterans were compared to non-GW Veterans, no significant differences were found in mortality associated with brain cancer, amyotrophic lateral sclerosis, Parkinson's disease and multiple sclerosis. However, GW Veterans potentially exposed to nerve agents for 2 or more days (i.e., at Khamisiyah) and GW veterans exposed to oil well fire smoke were at a 2.7 fold increase in risk for brain cancer. Another study (Kang et al., 2009) collected health information on 30,000 Veterans (15,000 GW Veterans and 15,000 Gulf-Era Veterans) using a

structured questionnaire. Fourteen years after deployment in 1991 GW Veterans compared to Gulf-Era Veterans reported a statistically significant higher prevalence of unexplained multi-symptom illnesses, chronic fatigue syndrome-like illness, posttraumatic stress disorder, functional impairment, use of health care and all mental disorders. Australian GW Veterans with multisymptom illness when compared to non-GW Veterans, showed high risk for major depression, posttraumatic stress disorder, increased unexplained stress disorder and functional impairment and poor quality of life. However, objective physical and laboratory measurements showed no difference. Two studies reported on risk of suicide. One study (Kaplan et al., 2009) analyzed suicide using firearms in 28,534 suicides from 2003-2006. They reported a 1.3 to 1.6 fold increase in suicides by firearms in male and female Veterans, respectively. The data also suggested that while younger Veterans (18-34 years) had a greater risk than others, older veterans from World War II, Korean Conflict, Vietnam Conflict and GW also showed more suicide by firearms than non-Veterans. A systematic review of the literature on the post-conflict injury-related mortality of service members who deployed to conflict zones found that injury-related mortality was elevated for veterans serving in the Persian Gulf War during 3 to 8 years of follow-up; much of the excess mortality among conflict-zone veterans was associated with motor vehicle events. The excess mortality decreased over time (Knapik et al., 2009).

Gulf War Illnesses

A study of 579 Navy construction workers (Seabees) showed that there was no relationship between antibodies for squalene, a natural organic compound found in the anthrax vaccine given service members, and reported multisymptom illnesses in those deployed to the 1990-1991 Gulf War. The authors concluded that squalene antibody status is not a part of multisymptom illnesses in Gulf War Veterans (Phillips et al., 2009).

Fibromyalgia (FM)

A study looking at the relationship between fibromyalgia and epileptic seizures found that the fibromyalgia suffers had more psychological distress than those without fibromyalgia (Johnson et al., 2009). A double blind, active-control, equivalency cross-over trial (Ware et al., 2009) showed that patients given nabilone, a synthetic cannaboid, a class of numerous compounds found in marijuana, was more effective in improving sleep in patients with fibromyalgia than the current therapy using amitriptyline. Another study (Feng et al., 2009) was designed to provide a fuller understanding of the role of genes in the development of fibromyalgia. The study found a link between rare missense variants of the MEFV gene, which encodes a protein involved with innate immunity that is responsive to environmental factors and a predisposition towards fibromyalgia.

Chronic Fatigue Syndrome (CFS)

A study (Fuite et al., 2008) of the interconnectedness of neuroendocrine and immune systems with CFS found a relationship between immune-mediated loss of thyroid function as a function of a blunted hypothalamic-pituitary-adrenal axis. An examination of the metabolic basis of CFS found that a strong correlation between the degree of mitochondrial dysfunction and the severity of the illness (Myhill et al., 2009). Another study found a cellular marker (8-hydroxy-deoxyguanosine) for oxidative damage to DNA, which may result from inflammatory and oxidative pathways, to be higher in patients with major depression, myalgic encephalomyelitis, or CFS. The authors speculated that this elevated marker, which is also seen in patients with atherosclerosis and neurodegeneration, may explain the increased cardiovascular morbidity found in patients with depression, myalgic encephalomyelitis or CFS (Maes et al., 2009).

F. Abstracts from Published Research

Amourette C, Lamproglou I, Barbier L, Fauquette W, Zoppe A, Viret R, Diserbo M (2009) Gulf War illness: Effects of repeated stress and pyridostigmine treatment on blood-brain barrier permeability and cholinesterase activity in rat brain. Behav Brain Res 203:207-214.

Abstract: After the first Persian Gulf War, many soldiers have complained of a variety of symptoms designated as "Gulf War Illness". Among several factors, implication of pyridostigmine (PB) in late cognitive dysfunction is highly likely. As a hypothesis to explain these behavioural disorders is a potentiation of the operational stress effects by pyridostigmine. We have previously described that repeated stress combined to pyridostigmine treatment induces learning dysfunction linked to genomic cerebral modifications [Barbier L, Diserbo M, Lamproglou I, Amourette C, Peinnequin A, Fauquette W. Repeated stress in combination with pyridostigmine: part II-changes in selected cerebral genes expression. Behav Brain Res 2009;197:292-300; Lamproglou I, Barbier L, Diserbo M, Fauvelle F, Fauquette W, Amourette C. Repeated stress in combination with pyridostigmine: part I-long-term behavioural consequences. Behav Brain Res 2009;197:301-10]. In the present study, using the same experimental model, we attempted to determine if such modifications are linked to a central passage of pyridostigmine under stress. Indeed it is known that exposure to stress can disrupt blood-brain barrier (BBB) and thereby increase the neurotoxicity induced by chemicals in many cerebral areas. Adult rats were subjected to repeated stress based on a modification of the pole climbing avoidance technique and treated daily by PB (1.5mg/kg/day, oral in water), for two 5-day periods separated by 2-day rest. Just after the last stress session, ^{3}H-pyridostigmine was administered as a tracer to evaluate BBB breakdown. In brain micro-punches and brain coronal cryosections, we failed to detect any radioactivity in animals chronically stressed and treated by pyridostigmine. Accordingly, no change of ChE activity was noted in any brain area studied. It thus appears that, in our experimental model, pyridostigmine induces effects on central nervous system, but these effects do not seem to be mediated by a central passage of pyridostigmine linked to a BBB opening under stress. These results suggest that pyridostigmine may have central effects, under stress, via indirect mechanisms emerging from a peripheral pathway.

Arfsten DP, Still KR, Wilfong ER, Johnson EW, McInturf SM, Eggers JS, Schaeffer DJ, Bekkedal MY (2009) Two-generation reproductive toxicity study of implanted depleted uranium (DU) in CD rats. J Toxicol Environ Health A 72:410-427.

Abstract: Depleted uranium (DU) munitions and armor plating have been used in several conflicts over the last 17 yr, including the Persian Gulf War and the Iraq War. Because of its effectiveness and availability, DU will continue to be used in military applications into the foreseeable future. There is much controversy over the use of DU in weapons and equipment because of its potential radiological and toxic hazards, and there is concern over the chronic adverse health effects of embedded DU shrapnel in war veterans and bystanders. This study evaluated the effects of long-term implantation of DU on the reproductive success of F0 generation adults and development and survival of subsequent F1 and F2 generations in a two-generation reproductive toxicity study. F0 generation Sprague-Dawley rats, 8 wk of age, were surgically implanted with 0, 4, 8, 12, or 20 DU pellets (1 x 2 mm). Inert implant control animals were implanted with 12 or 20 tantallum (Ta) pellets. The F0 generation was then mated at 120 d post DU implantation. In the F0 generation, when measured on postimplantation d 27 and 117, uranium was present in the urine of DU-implanted animals in a dose-dependent manner. F0 reproductive success was similar across treatment groups and the maternal retrieval test revealed no changes in maternal behavior. DU implantation exerted no effect on the survival, health, or well-being of the F0 generation. Necropsy results of F0 animals were negative with the exception of a marked inflammatory response surrounding the implanted DU pellets. For the F1 generation, measures of F1 development through postnatal day (PND) 20 were unremarkable and no gross abnormalities were observed in F1 offspring. No uranium was detected in whole-body homogenates of PND 4 or PND 20 pups. Necropsy findings of F1 PND 20 pups were negative and no instances of ribcage malformation were observed in F1 PND 20 pups. Body weight and body weight gain of F1 rats through PND 120 were similar across treatment groups. Eight of 414 F1 animals observed from PND 20 to 120 died of unknown causes; 7 were from litters of DU-implanted F0 mating pairs. F1 mating success at 10 wk of age was an overall 70% compared with 91% for F0 mating pairs. Mating success was similar between F1 animals derived from DU-implanted F0 adults and those derived from F0 implant control adults suggesting that the comparatively low mating success was not due to F1 DU exposure. The gestational index of F1 animals derived from mid-dose F0 mating pairs was found to be lower compared with F1 controls. The average gestation duration of F1 animals derived from high-dose F0 mating pairs was found to be significantly longer than F1 controls. F1 sperm motility analyses did not differ among experimental groups and no gross abnormalities were identified at necropsy among surviving F1 animals at PND 120. Histopathology of kidneys, spleen, thymus, bone marrow, ovaries, and testes of F1 high-dose animals did not differ from F1 controls. F1 high-dose females had significantly higher mean relative liver and heart weights compared with F1 controls; the biological relevance of this finding could not be determined. For the F2 generation, measures of F2 development through PND 20 were unremarkable and no gross abnormalities were

observed in F2 offspring. Necropsy findings of F2 PND 20 pups were negative and no instances of ribcage malformation were observed in F2 PND 20 pups. Body weight and body weight gain of F2 rats through PND 90 were similar across treatment groups. Mean relative heart weights of males derived from high-dose F0 parents were significantly lower compared with F2 controls. Sperm motility and concentration analysis of F2 males at PND 90 were similar across F2 groups. Overall, the consistent absence of positive findings in this study seems to suggest that DU is not a significant reproductive or developmental hazard, particularly when one considers that mid- and high-dose rats were implanted with the equivalent of 0.3 and 0.5 lb of DU in a 70-kg human, respectively. However, the findings that seven of eight F1 adults that died postweaning were from DU-implanted F0 mating pairs, and that mean relative heart weights were elevated in high-dose F1 and F2 pups, suggest conservatism is warranted in characterizing the reproductive and teratogenic hazards of embedded DU until further studies are completed.

Barbier L, Diserbo M, Lamproglou I, Amourette C, Peinnequin A, Fauquette W (2009) Repeated stress in combination with pyridostigmine Part II: changes in cerebral gene expression. Behav Brain Res 197:292-300.
Abstract: Organophosphates (OP) represent a potential threat in terrorism or during military conflicts. Due to its faculty to protect cholinesterase (ChE) activity against irreversible inactivation by OP, pyridostigmine bromide (PB) was used as a prophylaxis treatment during the first Persian Gulf War. To explain dysfunctions reported by Gulf War Veterans (GWV), it was suggested a potentiation of the operational stress effects by PB given to soldiers. Our companion paper (see part 1 in the same journal issue) describes that PB treatment administered in repeated stress conditions results in long-term perturbations of learning and social behaviour. The present paper examines, in adult male Wistar rats, consequences of the association of repeated stress and PB treatment on gene expression in hypothalamus and hippocampus. PB treatment (1.5 mg/kg/day) was orally administered 30 min before each stress session to inhibit 40% of blood ChE as recommended by NATO. 10 days of stress alone induce a decrease in hypothalamic Il-1alpha expression. Treatment with PB alone increases mineralocorticoid receptor expression in hypothalamus which means that PB may thus modify stress perception by animals. Stressed-PB animals showed increase in hippocampal expression of BDNF, TrkB and CamKIIalpha, three genes implicated in memory development. As a supplement to previous studies showing behavioural and biochemical effects of the association of stress with PB, our data reveal that behavioural effects of this association may be linked with genomic changes in hippocampus. Mechanisms underlying these modifications and their link with memory disturbances reported by GWV remain to be further determined.

Barth SK, Kang HK, Bullman TA, Wallin MT (2009) Neurological mortality among U.S. veterans of the Persian Gulf War: 13-year follow-up. Am J Ind Med 52:663-670.
Abstract: BACKGROUND: This study focuses on long-term mortality, specifically brain cancer, amyotrophic lateral sclerosis (ALS), Parkinson's disease, and multiple sclerosis (MS) of 621,902 veterans who served in the 1990-1991 Persian Gulf War (GW), and 746,248 non-GW veterans. METHODS: Follow-up began with the date the veteran left the GW theater or May 1, 1991 and ended with the date of death or December 31, 2004. Cox proportional hazard models were used for analyses. RESULTS: Adjusted mortality rate ratios (aRR) of GW veterans compared to non-GW veterans were not statistically significant for brain cancer (aRR = 0.90, 95% confidence interval (CI): 0.73, 1.11), MS (aRR = 0.61, 95% CI: 0.23, 1.63), Parkinson's disease (aRR = 0.71, 95% CI: 0.17, 2.99), or ALS (aRR = 0.96, 95% CI: 0.56, 1.62). GW veterans potentially exposed to nerve agents for 2 or more days and GW veterans exposed to oil well fire smoke were at increased risk for brain cancer mortality (aRR = 2.71, 95% CI: 1.25, 5.87; aRR = 1.81, 95% CI: 1.00, 3.27; respectively). CONCLUSIONS: The risk of death due to ALS, MS, Parkinson's disease, and brain cancer was not associated with 1991 GW service in general. However, GW veterans potentially exposed to nerve agents at Khamisiyah, Iraq, and to oil well fire smoke had an increased risk of mortality due to brain cancer.

Cheng YS, Kenoyer JL, Guilmette RA, Parkhurst MA (2009) Physicochemical characterization of Capstone depleted uranium aerosols II: particle size distributions as a function of time. Health Phys 96:266-275.
Abstract: The Capstone Depleted Uranium (DU) Aerosol Study, which generated and characterized aerosols containing DU from perforation of armored vehicles with large-caliber DU penetrators, incorporated a sampling protocol to evaluate particle size distributions. Aerosol particle size distribution is an important parameter that influences aerosol transport and deposition processes as well as the dosimetry of the inhaled particles. These aerosols were collected on cascade impactor substrates using a pre-established time sequence following the firing event to analyze the uranium concentration and particle size of the aerosols as a function of time. The impactor substrates were analyzed using proportional counting, and the derived uranium content of each served as input to the evaluation of particle size distributions. Activity median aerodynamic diameters (AMADs) of the particle size distributions were evaluated using unimodal and bimodal models. The particle size data from the impactor measurements were quite variable. Most size distributions measured in the test based on activity had bimodal size distributions with a small particle size mode in the range of between 0.2 and 1.2 microm and a large size mode between 2 and 15 microm. In general, the evolution of

particle size over time showed an overall decrease of average particle size from AMADs of 5 to 10 microm shortly after perforation to around 1 microm at the end of the 2-h sampling period. The AMADs generally decreased over time because of settling. Additionally, the median diameter of the larger size mode decreased with time. These results were used to estimate the dosimetry of inhaled DU particles.

Cox PA, Richer R, Metcalf JS, Banack SA, Codd GA, Bradley WG (2009) Cyanobacteria and BMAA exposure from desert dust: a possible link to sporadic ALS among Gulf War veterans. Amyotroph Lateral Scler 10 Suppl 2:109-117.

Abstract: Veterans of the 1990-1991 Gulf War have been reported to have an increased incidence of amyotrophic lateral sclerosis (ALS) compared to personnel who were not deployed. An excess of ALS cases was diagnosed in Gulf War veterans younger than 45 years of age. Increased ALS among Gulf War veterans appears to be an outbreak time-limited to the decade following the Gulf War. Seeking to identify biologically plausible environmental exposures, we have focused on inhalation of cyanobacteria and cyanotoxins carried by dust in the Gulf region, particularly Qatar. Cyanobacterial crusts and mats are widespread in the deserts of Qatar, occupying up to 56% of the available area in some microhabitats. These cyanobacterial crusts, which help bind the desert sands, are dormant throughout most of the year, but during brief spring rains actively photosynthesize. When disturbed by vehicular traffic or other military activities, the dried crusts and mats can produce significant dust. Using HPLC/FD, an amino acid analyzer, UPLC/MS, and triple quadrupole LC/MS/MS we find that the dried crusts and mats contain neurotoxic cyanobacterial toxins, including beta-N-methylamino-L-alanine (BMAA) and 2,4 diaminobutyric acid (DAB). If dust containing cyanobacteria is inhaled, significant exposure to BMAA and other cyanotoxins may occur. We suggest that inhalation of BMAA, DAB, and other aerosolized cyanotoxins may constitute a significant risk factor for the development of ALS and other neurodegenerative diseases.

Dassanayake T, Gawarammana IB, Weerasinghe V, Dissanayake PS, Pragaash S, Dawson A, Senanayake N (2009) Auditory event-related potential changes in chronic occupational exposure to organophosphate pesticides. Clin Neurophysiol 120:1693-1698.

Abstract: OBJECTIVE: To determine whether chronic occupational exposure to organophosphates (OP) pesticides leads to cognitive impairment using event-related potentials (ERPs). METHODS: ERPs of 38 vegetable farmers applying OP pesticides and 35 controls were recorded using an auditory oddball paradigm. The N1, P2, N2 and P300 ERP components and the number of counting errors were compared between the groups. RESULTS: The farmers made significantly more counting errors than controls in the oddball task. The mixed model ANOVA of component latencies revealed a significant componentxgroup interaction, suggesting farmers had a greater delay in later ERP components. Intergroup comparisons of individual components showed significant delays in N2 and P300 latencies. Subsequent ANCOVA showed significant P300 delay even after adjusting for the latency of the preceding component, N2. Intergroup differences of P300 amplitudes were not significant, although there was limited evidence of a difference in scalp topography. CONCLUSION: Our findings indicate that chronic low-level occupational exposure to OP pesticides is associated with progressively increasing delay in successive ERP components, particularly P300. SIGNIFICANCE: Chronic exposure to OP pesticides may delay the neurophysiological processes underlying early stages of selective attention and late stages of sensory information processing that include stimulus evaluation and updating of working memory.

Daxon EG, Parkhurst MA, Melanson MA, Roszell LE (2009) Applications of Capstone depleted uranium aerosol risk data to military combat risk management. Health Phys 96:380-392.

Abstract: Risks to personnel engaged in military operations include not only the threat of enemy firepower but also risks from exposure to other hazards such as radiation. Combatant commanders of the U.S. Army carefully weigh risks of casualties before implementing battlefield actions using an established paradigm that takes these risks into consideration. As a result of the inclusion of depleted uranium (DU) anti-armor ammunition in the conventional (non-nuclear) weapons arsenal, the potential for exposure to DU aerosols and its associated chemical and radiological effects becomes an element of the commanders' risk assessment. The Capstone DU Aerosol Study measured the range of likely DU oxide aerosol concentrations created inside a combat vehicle perforated with a DU munition, and the Capstone Human Health Risk Assessment (HHRA) estimated the associated doses and calculated risks. This paper focuses on the development of a scientific approach to adapt the risks from DU's non-uniform dose distribution within the body using the current U.S. Department of Defense radiation risk management approach. The approach developed equates the Radiation Exposure Status categories to the estimated radiological risks of DU and makes use of the Capstone-developed Renal Effects Group as a measure of chemical risk from DU intake. Recommendations are provided for modifying Army guidance and policy in order to better encompass the potential risks from DU aerosol inhalation during military operations.

Dorsey CD, Engelhardt SM, Squibb KS, McDiarmid MA (2009) Biological monitoring for depleted uranium exposure in U.S. Veterans. Environ Health Perspect 117:953-956.
Abstract: BACKGROUND: As part of an ongoing medical surveillance program for U.S. veterans exposed to depleted uranium (DU), biological monitoring of urine uranium (U) concentrations is offered to any veteran of the Gulf War and those serving in more recent conflicts (post-Gulf War veterans). OBJECTIVES: Since a previous report of surveillance findings in 2004, an improved methodology for determination of the isotopic ratio of U in urine (^{235}U:^{238}U) has been developed and allows for more definitive evaluation of DU exposure. This report updates previous findings. METHODS: Veterans provide a 24-hr urine specimen and complete a DU exposure questionnaire. Specimens are sent to the Baltimore Veterans Affairs Medical Center for processing. Uranium concentration and isotopic ratio are measured using ICP-MS at the Armed Forces Institute of Pathology. RESULTS: Between January 2003 and June 2008, we received 1,769 urine specimens for U analysis. The mean urine U measure was 0.009 μU/g creatinine. Mean urine U concentrations for Gulf War and post-Gulf War veterans were 0.008 and 0.009 μU/g creatinine, respectively. Only 3 of the 1,700 (0.01%) specimens for which we completed isotopic determination showed evidence of DU. Exposure histories confirmed that these three individuals had been involved in "friendly fire" incidents involving DU munitions or armored vehicles. CONCLUSIONS: No urine U measure with a "depleted" isotopic signature has been detected in U.S. veterans without a history of retained DU embedded fragments from previous injury. These findings suggest that future DU-related health harm is unlikely in veterans without DU fragments.

Feng J, Zhang Z, Li W, Shen X, Song W, Yang C, Chang F, Longmate J, Marek C, St Amand RP, Krontiris TG, Shively JE, Sommer SS (2009) Missense mutations in the MEFV gene are associated with fibromyalgia syndrome and correlate with elevated IL-1beta plasma levels. PLoS One 4:e8480.
Abstract: BACKGROUND: Fibromyalgia syndrome (FMS), a common, chronic, widespread musculoskeletal pain disorder found in 2% of the general population and with a preponderance of 85% in females, has both genetic and environmental contributions. Patients and their parents have high plasma levels of the chemokines MCP-1 and eotaxin, providing evidence for both a genetic and an immunological/inflammatory origin for the syndrome (Zhang et al., 2008, Exp. Biol. Med. 233: 1171-1180). METHODS AND FINDINGS: In a search for a candidate gene affecting inflammatory pathways, among five screened in our patient samples (100 probands with FMS and their parents), we found 10 rare and one common alleles for MEFV, a gene in which various compound heterozygous mutations lead to Familial Mediterranean Fever (FMF). A total of 2.63 megabases of genomic sequence of the MEFV gene were scanned by direct sequencing. The collection of rare missense mutations (all heterozygotes and tested in the aggregate) had a significant elevated frequency of transmission to affecteds ($p = 0.0085$, one-sided, exact binomial test). Our data provide evidence that rare missense variants of the MEFV gene are, collectively, associated with risk of FMS and are present in a subset of 15% of FMS patients. This subset had, on average, high levels of plasma IL-1beta ($p = 0.019$) compared to FMS patients without rare variants, unaffected family members with or without rare variants, and unrelated controls of unknown genotype. IL-1beta is a cytokine associated with the function of the MEFV gene and thought to be responsible for its symptoms of fever and muscle aches. CONCLUSIONS: Since misregulation of IL-1beta expression has been predicted for patients with mutations in the MEFV gene, we conclude that patients heterozygous for rare missense variants of this gene may be predisposed to FMS, possibly triggered by environmental factors.

Friedl KE, Grate SJ, Proctor SP (2009) Neuropsychological issues in military deployments: lessons observed in the DoD Gulf War Illnesses Research Program. Mil Med 174:335-346.
Abstract: The U.S. Department of Defense invested $150 M to investigate undiagnosed Gulf War Illnesses (GWI) and twice that amount in post hoc clinical management. No new disease syndrome was identified, but the research produced new understanding and awareness of important psychosocial and neurotoxicological interactions that represented a difficult and relatively untapped frontier in biomedical research, especially concerning chronic multisymptom illnesses. Some specific Gulf War issues such as effects of depleted uranium, Leishmania diagnosis and treatment, and pesticide and prophylactic drug interactions have been intensively investigated; remaining priorities for further investigation include: markers of neurologic change (e.g., neuroimaging, neuropsychological testing), interactions between psychological resilience and neurotoxicity, structure-function relationships of neurotoxins with neurodegenerative disease potential, and predictors of individual susceptibility. The primary conclusions from the program are that no specific neurotoxic chemical has been identified that explains the chronic multisymptom illness observed but wellness of service members in future deployments may be better sustained based on continuing research on preexposure health baselining, fitness and health-damaging behaviors, and stress resilience. The many scientific discoveries and accomplishments of the GWI research effort have advanced military medical science, provided a solid basis on which to build future protections against health and performance risks to the warfighter, and improved the ability to respond to future deployment health issues.

Fuite J, Vernon SD, Broderick G (2008) Neuroendocrine and immune network re-modeling in chronic fatigue syndrome: an exploratory analysis. Genomics 92:393-399.
Abstract: This work investigates the significance of changes in association patterns linking indicators of neuroendocrine and immune activity in patients with chronic fatigue syndrome (CFS). Gene sets preferentially expressed in specific immune cell isolates were integrated with neuroendocrine data from a large population-based study. Co-expression patterns linking immune cell activity with hypothalamic-pituitary-adrenal (HPA), thyroidal (HPT) and gonadal (HPG) axis status were computed using mutual information criteria. Networks in control and CFS subjects were compared globally in terms of a weighted graph edit distance. Local re-modeling of node connectivity was quantified by node degree and eigenvector centrality measures. Results indicate statistically significant differences between CFS and control networks determined mainly by re-modeling around pituitary and thyroid nodes as well as an emergent immune sub-network. Findings align with known mechanisms of chronic inflammation and support possible immune-mediated loss of thyroid function in CFS exacerbated by blunted HPA axis responsiveness.

Genovese RF, Mioduszewski RJ, Benton BJ, Pare MA, Cooksey JA (2009) Behavioral evaluation of rats following low-level inhalation exposure to sarin. Pharmacol Biochem Behav 91:517-525.
Abstract: We evaluated the effects, in rats, of single and multiple low-level inhalation exposures to sarin. Rats were trained on a variable-interval, 56 s (VI56) schedule of food reinforcement and then exposed to sarin vapor (1.7-4.0 mg/m^3 x 60 min) or air control. The exposures did not produce clinical signs of toxicity other than miosis. Subsequently, performance on the VI56 and acquisition of a radial-arm maze spatial memory task was evaluated over approximately 11 weeks. Single exposures did not affect performance on the VI56 and had little effect on acquisition of the radial-arm maze task. Multiple exposures (4.0 mg/m^3 x 60 min/day x 3) disrupted performance on the VI56 schedule during the initial post-exposure sessions. The disruption, however, resolved after several days. Multiple exposures also produced a deficit on the radial-arm maze task in that sarin-exposed rats tended to take it longer to complete the maze and to make more errors. The deficit, however, resolved during the first three weeks of acquisition. These results demonstrate that in rats, inhalation exposure to sarin at levels below those causing overt signs of clinical toxicity can produce cognitive and performance deficits. Furthermore, the observed deficits do not appear to be persistent.

Golier JA, Schmeidler J, Yehuda R (2009) Pituitary response to metyrapone in Gulf War veterans: relationship to deployment, PTSD and unexplained health symptoms. Psychoneuroendocrinology 34:1338-1345.
Abstract: OBJECTIVE: Gulf War deployment has been associated with a distinct neuroendocrine profile characterized by low 24h basal ACTH levels and enhanced cortisol and ACTH suppression to low-dose dexamethasone. The metyrapone stimulation test was performed to further characterize hypothalamic-pituitary activity in Gulf War veterans (GWV) and its relationship to unexplained medical symptoms and post-traumatic stress disorder (PTSD). METHOD: Eleven GWV without PTSD, 18 GWV with PTSD and 15 healthy subjects not exposed to the Gulf War theater (non-exposed) underwent the metyrapone stimulation test, which inhibits cortisol synthesis, impairs cortisol-mediated negative feedback inhibition and in turn increases levels of ACTH and 11-deoxycortisol, a cortisol precursor. These hormones were measured at baseline (7:00 a.m.) and at intervals (from 8:00 a.m. to 4:00 p.m.) following the administration of metyrapone 750mg orally at 7:05 a.m. and at 10:05 a.m. RESULTS: There were group differences in the ACTH response despite similar cortisol and 11-deoxycortisol responses to metyrapone. GWV without PTSD had a significantly attenuated ACTH response compared to non-exposed subjects; GWV with PTSD had a significantly higher ACTH response than GWV without PTSD but did not differ from non-exposed subjects. Among GWV, unexplained medical health symptoms (e.g., neurological, musculoskeletal, cardiac, and pulmonary symptoms) and PTSD symptoms were significantly positively associated with the ACTH response to metyrapone. CONCLUSION: Gulf War deployment is associated with a substantially lower ACTH response to metyrapone. In contrast, unexplained health symptoms and PTSD in Gulf War veterans are associated with relatively greater hypothalamic-pituitary activity which may reflect increased CRF activity and is evident only in consideration of deployment effects. This pattern of differences suggests either that Gulf War deployment and its associated exposures results in enduring changes in pituitary function or that reduced hypothalamic-pituitary activity protects against the development of PTSD and other deployment-related health problems.

Golomb BA (2008) Acetylcholinesterase inhibitors and Gulf War illnesses. Proc Natl Acad Sci U S A 105:4295-4300.
Abstract: 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.

Grigoryan H, Schopfer LM, Thompson CM, Terry AV, Masson P, Lockridge O (2008) Mass spectrometry identifies covalent binding of soman, sarin, chlorpyrifos oxon, diisopropyl fluorophosphate, and FP-biotin to tyrosines on tubulin: a potential mechanism of long term toxicity by organophosphorus agents. Chem Biol Interact 175:180-186.
Abstract: Chronic low dose exposure to organophosphorus poisons (OP) results in cognitive impairment. Studies in rats have shown that OP interfere with microtubule polymerization. Since microtubules are required for transport of nutrients from the nerve cell body to the nerve synapse, it has been suggested that disruption of microtubule function could explain the learning and memory deficits associated with OP exposure. Tubulin is a major constituent of microtubules. We tested the hypothesis that OP bind to tubulin by treating purified bovine tubulin with sarin, soman, chlorpyrifos oxon, diisopropylfluorophosphate, and 10-fluoroethoxyphosphinyl-N-biotinamidopentyldecanamide (FP-biotin). Tryptic peptides were isolated and analyzed by mass spectrometry. It was found that OP bound to tyrosine 83 of alpha tubulin in peptide TGTYR, tyrosine 59 in beta tubulin peptide YVPR, tyrosine 281 in beta tubulin peptide GSQQYR, and tyrosine 159 in beta tubulin peptide EEYPDR. The OP reactive tyrosines are located either near the GTP binding site or within loops that interact laterally with protofilaments. It is concluded that OP bind covalently to tubulin, and that this binding could explain cognitive impairment associated with OP exposure.

Grigoryan H, Li B, Xue W, Grigoryan M, Schopfer LM, Lockridge O (2009) Mass spectral characterization of organophosphate-labeled lysine in peptides. Anal Biochem 394:92-100.
Abstract: Organophosphate (OP) esters bind covalently to the active site serine of enzymes in the serine hydrolase family. Recently, mass spectrometry identified covalent binding of OPs to tyrosine in a wide variety of proteins when purified proteins were incubated with OPs. In the current work, manual inspection of tandem mass spectrometry (MS/MS) data led to the realization that lysines also make a covalent bond with OPs. OP-labeled lysine residues were found in seven proteins that had been treated with either chlorpyrifos oxon (CPO) or diisopropylfluorophosphate (DFP): human serum albumin (K212, K414, K199, and K351), human keratin 1 (K211 and K355), human keratin 10 (K163), bovine tubulin alpha (K60, K336, K163, K394, and K401), bovine tubulin beta (K58), bovine actin (K113, K291, K326, K315, and K328), and mouse transferrin (K296 and K626). These results suggest that OP binding to lysine is a general phenomenon. Characteristic fragments specific for CPO-labeled lysine appeared at 237.1, 220.0, 192.0, 163.9, 128.9, and 83.9amu. Characteristic fragments specific for DFP-labeled lysine appeared at 164.0, 181.2, and 83.8amu. This new OP-binding motif to lysine suggests new directions to search for mechanisms of long-term effects of OP exposure and in the search for biomarkers of OP exposure.

Guilmette RA, Miller G, Parkhurst MA (2009) Capstone depleted uranium aerosol biokinetics, concentrations, and doses. Health Phys 96:328-342.
Abstract: One of the principal goals of the Capstone Depleted Uranium (DU) Aerosol Study was to quantify and characterize DU aerosols generated inside armored vehicles by perforation with a DU penetrator. This study consequently produced a database in which the DU aerosol source terms were specified both physically and chemically for a variety of penetrator-impact geometries and conditions. These source terms were used to calculate radiation doses and uranium concentrations for various scenarios as part of the Capstone Human Health Risk Assessment (HHRA). This paper describes the scenario-related biokinetics of uranium, and summarizes intakes, chemical concentrations to the organs, and E(50) and HT(50) for organs and tissues based on exposure scenarios for personnel in vehicles at the time of perforation as well as for first responders. For a given exposure scenario (duration time and breathing rates), the range of DU intakes among the target vehicles and shots was not large, about a factor of 10, with the lowest being for a ventilated operational Abrams tank and the highest being for an unventilated Abrams with DU penetrator perforating DU armor. The ranges of committed effective doses were more scenario-dependent than were intakes. For example, the largest range, a factor of 20, was shown for scenario A, a 1 min exposure, whereas, the range was only a factor of two for the first-responder scenario (E). In general, the committed effective doses were found to be in the tens of mSv. The risks ascribed to these doses are discussed separately.

Guilmette RA, Cheng YS (2009) Physicochemical characterization of Capstone depleted uranium aerosols IV: in vitro solubility analysis. Health Phys 96:292-305.
Abstract: As part of the Capstone Depleted Uranium (DU) Aerosol Study, the solubility of selected aerosol samples was measured using an accepted in vitro dissolution test system. This static system was employed along with a SUF

(synthetic ultrafiltrate) solvent, which is designed to mimic the physiological chemistry of extracellular fluid. Using sequentially obtained solvent samples, the dissolution behavior over a 46-d test period was evaluated by fitting the measurement data to two- or three-component negative exponential functions. These functions were then compared with Type M and S absorption taken from the International Commission on Radiological Protection Publication 66 Human Respiratory Tract Model. The results indicated that there was a substantial variability in solubility of the aerosols, which in part depended on the type of armor being impacted by the DU penetrator and the particle size fraction being tested. Although some trends were suggested, the variability noted leads to uncertainties in predicting the solubility of other DU-based aerosols. Nevertheless, these data provide a useful experimental basis for modeling the intake-dose relationships for inhaled DU aerosols arising from penetrator impact on armored vehicles.

Hahn FF, Roszell LE, Daxon EG, Guilmette RA, Parkhurst MA (2009) Radiological risk assessment of Capstone depleted uranium aerosols. Health Phys 96:352-362.
Abstract: Assessment of the health risk from exposure to aerosols of depleted uranium (DU) is an important outcome of the Capstone aerosol studies that established exposure ranges to personnel in armored combat vehicles perforated by DU munitions. Although the radiation exposure from DU is low, there is concern that DU deposited in the body may increase cancer rates. Radiation doses to various organs of the body resulting from the inhalation of DU aerosols measured in the Capstone studies were calculated using International Commission on Radiological Protection (ICRP) models. Organs and tissues with the highest calculated committed equivalent 50-y doses were lung and extrathoracic tissues (nose and nasal passages, pharynx, larynx, mouth, and thoracic lymph nodes). Doses to the bone surface and kidney were about 5 to 10% of the doses to the extrathoracic tissues. Organ-specific risks were estimated using ICRP and U.S. Environmental Protection Agency (EPA) methodologies. Risks for crewmembers and first responders were determined for selected scenarios based on the time interval of exposure and for vehicle and armor type. The lung was the organ with the highest cancer mortality risk, accounting for about 97% of the risks summed from all organs. The highest mean lifetime risk for lung cancer for the scenario with the longest exposure time interval (2 h) was 0.42%. This risk is low compared with the natural or background risk of 7.35%. These risks can be significantly reduced by using an existing ventilation system (if operable) and by reducing personnel time in the vehicle immediately after perforation.

Haley RW, Spence JS, Carmack PS, Gunst RF, Schucany WR, Petty F, Devous MD, Sr., Bonte FJ, Trivedi MH (2009) Abnormal brain response to cholinergic challenge in chronic encephalopathy from the 1991 Gulf War. Psychiatry Res 171:207-220.
Abstract: Several case definitions of chronic illness in veterans of the 1991 Persian Gulf War have been linked epidemiologically with environmental exposure to cholinesterase-inhibiting chemicals, which cause chronic changes in cholinergic receptors in animal models. Twenty-one chronically ill Gulf War veterans (5 with symptom complex 1, 11 with complex 2, and 5 with complex 3) and 17 age-, sex- and education-matched controls, underwent an 99mTc-HMPAO-SPECT brain scan following infusion of saline and >48 h later a second scan following infusion of physostigmine in saline. From each SPECT image mean normalized regional cerebral blood flow (nrCBF) from 39 small blocks of correlated voxels were extracted with geostatistical spatial modeling from eight deep gray matter structures in each hemisphere. Baseline nrCBF in symptom complex 2 was lower than controls throughout deep structures. The change in nrCBF after physostigmine (challenge minus baseline) was negative in complexes 1 and 3 and controls but positive in complex 2 in some structures. Since effects were opposite in different groups, no finding typified the entire patient sample. A hold-out discriminant model of nrCBF from 17 deep brain blocks predicted membership in the clinical groups with sensitivity of 0.95 and specificity of 0.82. Gulf War-associated chronic encephalopathy in a subset of veterans may be due to neuronal dysfunction, including abnormal cholinergic response, in deep brain structures.

Hao Y, Li R, Leng Y, Ren J, Liu J, Ai G, Xu H, Su Y, Cheng T (2009) A study assessing the genotoxicity in rats after chronic oral exposure to a low dose of depleted uranium. J Radiat Res (Tokyo) 50:521-528.
Abstract: PURPOSE: The aim of this study was to evaluate the potential genotoxicity induced by chronic oral exposure to depleted uranium (DU). MATERIALS AND METHODS: Weanling Wistar rats (F(0)), 50/sex/group, were exposed to DU in food at doses of 0, 4, or 40 mg kg(-1)day(-1) for four months. They were subsequently mated, resulting in the birth of F(1) rats. Fifty F(l) weanlings/sex/group were exposed for four months to the same dose levels as their parents. After four months, the uranium content in the tissues, the potential damage to the genetic material, and pathomorphological changes of the testicles were observed in both F(0) and F(1) rats. The genotoxicity of DU was evaluated by the following methods: sperm abnormality assessment, the bone-marrow micronucleus test, and the comet assay. RESULTS: Uranium content in F(1) rats was significantly higher than that in F(0) rats in both the kidney and ovary ($p < 0.05$). The sperm abnormality rate, marrow cell micronuclei rate, comet tail length, and tailed cell percentage increased in each treatment group in each generation compared with the control group ($p < 0.05$). When comparing F(1)

with F(0) rats, significant differences were detected for most of the indicators, with F(1) rats always exhibiting more damage ($p < 0.05$). With regard to pathomorphological changes in the testicles, the sperm displayed atypical changes, including thickening of the anachromasis nucleolus, which seemed to be more severe in F(1) rats. CONCLUSION: Genotoxicity may be induced in rats after chronic oral exposure to a low dose of DU.

Heppner PS, Crawford EF, Haji UA, Afari N, Hauger RL, Dashevsky BA, Horn PS, Nunnink SE, Baker D (2009) The Association of Posttraumatic Stress Disorder and Metabolic Syndrome: A Study of Increased Health Risk in Veterans. BMC Med. 7:1-8.
Abstract: BACKGROUND: There is accumulating evidence for a link between trauma exposure, posttraumatic stress disorder (PTSD) and diminished health status. To assess PTSD-related biological burden, we measured biological factors that comprise metabolic syndrome, an important established predictor of morbidity and mortality, as a correlate of long-term health risk in PTSD. METHODS: We analyzed clinical data from 253 male and female veterans, corresponding to five factors linked to metabolic syndrome (systolic and diastolic blood pressure, waist-to-hip ratio and fasting measures of high-density lipoprotein (HDL) cholesterol, serum triglycerides and plasma glucose concentration). Clinical cut-offs were defined for each biological parameter based on recommendations from the World Health Organization and the National Cholesterol Education Program. Controlling for relevant variables including sociodemographic variables, alcohol/substance/nicotine use and depression, we examined the impact of PTSD on metabolic syndrome using a logistic regression model. RESULTS: Two-fifths (40%) of the sample met criteria for metabolic syndrome. Of those with PTSD ($n = 139$), 43% met criteria for metabolic syndrome. The model predicted metabolic syndrome well (-2 log likelihood = 316.650, chi-squared = 23.731, $p = 0.005$). Veterans with higher severity of PTSD were more likely to meet diagnostic criteria for metabolic syndrome (Wald = 4.76, $p = 0.03$). CONCLUSION: These findings provide preliminary evidence linking higher severity of PTSD with risk factors for diminished health and increased morbidity, as represented by metabolic syndrome.

Holmes TD, Guilmette RA, Cheng YS, Parkhurst MA, Hoover MD (2009) Aerosol sampling system for collection of Capstone depleted uranium particles in a high-energy environment. Health Phys 96:221-237.
Abstract: The Capstone Depleted Uranium (DU) Aerosol Study was undertaken to obtain aerosol samples resulting from a large-caliber DU penetrator striking an Abrams or Bradley test vehicle. The sampling strategy was designed to (1) optimize the performance of the samplers and maintain their integrity in the extreme environment created during perforation of an armored vehicle by a DU penetrator, (2) collect aerosols as a function of time post perforation, and (3) obtain size-classified samples for analysis of chemical composition, particle morphology, and solubility in lung fluid. This paper describes the experimental setup and sampling methodologies used to achieve these objectives. Custom-designed arrays of sampling heads were secured to the inside of the target in locations approximating the breathing zones of the crew locations in the test vehicles. Each array was designed to support nine filter cassettes and nine cascade impactors mounted with quick-disconnect fittings. Shielding and sampler placement strategies were used to minimize sampler loss caused by the penetrator impact and the resulting fragments of eroded penetrator and perforated armor. A cyclone train was used to collect larger quantities of DU aerosol for measurement of chemical composition and solubility. A moving filter sample was used to obtain semicontinuous samples for DU concentration determination. Control for the air samplers was provided by five remotely located valve control and pressure monitoring units located inside and around the test vehicle. These units were connected to a computer interface chassis and controlled using a customized LabVIEW engineering computer control program. The aerosol sampling arrays and control systems for the Capstone study provided the needed aerosol samples for physicochemical analysis, and the resultant data were used for risk assessment of exposure to DU aerosol.

Johnson AL, Storzbach D, Binder LM, Barkhuizen A, Kent AW, Salinsky MC, Tun SM, Rohlman DS (2009) MMPI-2 profiles: Fibromyalgia Patients Compared to Epileptic and Non-Epileptic Seizure Patients. Clin Neuropsychol1-15.
Abstract: We compared MMPI-2 profiles of Gulf War veterans with fibromyalgia (FM) to epileptic seizure (ES) patients, psychogenic non-epileptic seizure (PNES) patients, and Gulf War veteran healthy controls. Both PNES and FM are medically unexplained conditions. In previous MMPI-2 research PNES patients were shown to have significantly higher Hs and Hy clinical scales than ES patients. In the present research the FM group had significantly higher Hs and Hy scale scores than both the ES group and the healthy control group. There was no significant difference between the FM and PNES Hs scale scores; however, the FM Hy scale score was significantly lower than the PNES Hy scale score. Present findings indicate a high level of psychological distress in the FM group.

Kang HK, Li B, Mahan CM, Eisen SA, Engel CC (2009) Health of US veterans of 1991 Gulf War: a follow-up survey in 10 years. J Occup Environ Med 51:401-410.
Abstract: OBJECTIVE: To assess periodically the health status of a cohort of 1991 Gulf War veterans by comparing

various health outcomes with those of their military peers who were not deployed to the Gulf. METHODS: We conducted a follow-up health survey to collect health information among population-based samples of 30,000 veterans (15,000 Gulf War veterans and 15,000 Gulf Era veterans) using a structured questionnaire. RESULTS: Gulf veterans reported significantly higher rates of unexplained multi-symptom illness, chronic fatigue syndrome-like illness, posttraumatic stress disorder, functional impairment, health care utilization, a majority of selected physical conditions and all mental disorders queried during the survey than did Gulf Era veteran controls. CONCLUSIONS: Fourteen years after deployment, 1991 Gulf War veterans continue to report a higher prevalence of many adverse health outcomes, compared with Gulf Era veterans.

Kaplan MS, McFarland BH, Huguet N (2009) Firearm suicide among veterans in the general population: findings from the national violent death reporting system. J Trauma 67:503-507.
Abstract: BACKGROUND: Military veterans are particularly vulnerable to suicide compared with their civilian peers. Scant attention has been devoted to the problem of firearm suicide among veterans, particularly women. The purpose of this study was to examine the rate, prevalence, and relative odds of firearm use among veteran suicide decedents in the general population. METHODS: The analyses are based on data derived from 28,534 suicide decedents from the 2003 to 2006 National Violent Death Reporting System. RESULTS: Across the age groups, male and female veterans had higher firearm suicide rates than nonveterans. Among males and females, younger veterans (18-34 years) had the highest firearm and total suicide rates. The male and female veteran suicide decedents were, respectively, 1.3 and 1.6 times more likely to use firearms relative to nonveterans after adjusting for age, marital status, race, and region of residence. CONCLUSIONS: Although violent death and the use of firearms are generally associated with men, the results reported here suggest that firearms among female veterans deserve particular attention among health professionals within and outside the veterans affairs system. In addition, the focus should not be exclusively on the Operation Enduring Freedom/Operation Iraqi Freedom military cohort but also on men and women who served in earlier combat theaters, including the Gulf war, Vietnam Era, Korean Conflict, and World War II.

Kasarskis EJ, Lindquist JH, Coffman CJ, Grambow SC, Feussner JR, Allen KD, Oddone EZ, Kamins KA, Horner RD (2009) Clinical aspects of ALS in Gulf War veterans. Amyotroph Lateral Scler 10:35-41.
Abstract: The increased incidence of ALS in military veterans of the first Persian Gulf War raised speculation that they may have a 'Persian Gulf' variant of ALS with atypical clinical features. Medical records of military veterans with ALS, previously identified in our epidemiological study, were evaluated for clinical features (age and site of onset, race, unexplained atypical findings) and ventilator-free survival. Comparisons between deployed versus non-deployed cohorts were made with deployment status based on designation by the Department of Defense Manpower Data Center (DMDC) or by self-report. Other than the young age of onset in both cohorts (40.8 years overall mean; 40.1 years for DMDC deployed, 41.2 years for DMDC non-deployed), review of the medical records failed to document any atypical features. After adjusting for bulbar onset, median survival from symptom onset in those > or =40 years of age was 35.5 months (2.96 years) compared to 64.7 months (5.39 years) in the group <40 years of age (hazard ratio (HR)=0.47, 95% CI 0.30-0.73, p=0.0006). After adjusting for age, median survival was 45.4 months (3.78 years) and 54.8 months (4.57 years) in bulbar- versus non-bulbar onset groups, respectively (HR=1.41, 95% CI 0.83-2.39, p=0.20). After adjusting for age and site of onset, deployed veterans had significantly shorter survival than non-deployed (40.2 vs. 57.0 months, HR=0.62, 95% CI 0.40-0.96, p=0.03) using DMDC data. In conclusion, although veterans developing ALS after deployment to the Persian Gulf in 1990-1991 exhibited otherwise typical clinical features, they experienced shorter ventilator-free survival than non-deployed veterans.

Kelsall HL, McKenzie DP, Sim MR, Leder K, Forbes AB, Dwyer (2009) Physical, psychological, and functional comorbidities of multisymptom illness in Australian male veterans of the 1991Gulf War. Am J Epidemiol 170:1048-1056 (Epub 2009 Sep 17).
Abstract: Multisymptom illness is more prevalent in 1991 Gulf War veterans than in military comparison groups; less is known about comorbidities. The authors compared physical, psychological, and functional comorbidities in Australian male Gulf War I veterans with those in actively (non-Gulf) deployed and nondeployed military personnel by using a questionnaire and medical assessment in 2000-2002. Multisymptom illness was more common in male Gulf War veterans than in the comparison group (odds ratio (OR) = 1.80, 95% confidence interval (CI): 1.48, 2.19). Stratifying by deployment status in the comparison group made little difference in this association. Gulf War veterans with multisymptom illness had increased psychiatric disorders, including major depression (OR = 6.31, 95% CI: 4.19, 9.52) and posttraumatic stress disorder (OR = 9.77, 95% CI: 5.39, 18.59); increased unexplained chronic fatigue (OR = 13.32, 95% CI: 7.70, 23.05); and more reported functional impairment and poorer quality of life, but objective physical and laboratory outcomes were similar to those for veterans without multisymptom illness. Similar patterns were found in the comparison groups; differences across the 3 groups were statistically significant for only hospitalization, obstructive

liver disease, and Epstein-Barr virus exposure. Multisymptom illness is more prevalent in Gulf War I veterans, but the pattern of comorbidities is similar for actively deployed and nondeployed military personnel.

Khan O, Shen Y, Bao F, Caon C, Tselis A, Latif Z, Zak I (2008) Long-term study of brain 1H-MRS study in multiple sclerosis: effect of glatiramer acetate therapy on axonal metabolic function and feasibility of long-Term H-MRS monitoring in multiple sclerosis. J Neuroimaging 18:314-319.
Abstract: Glatiramer acetate (GA) has several putative mechanisms of action with the potential of limiting sublethal axonal injury in the central nervous system (CNS). Brain proton magnetic resonance spectroscopy ((1)H-MRS) allows in vivo examination of axonal integrity by quantifying the neuronal marker N-acetylaspartate (NAA), often expressed as a ratio to creatine (Cr). We showed that treatment with GA led to improvement in NAA/Cr over a 2-year period. We now report the results of this ongoing study after 4 years of annual brain (1)H-MRS examinations. Compared to baseline, at year 4, patients receiving continuous GA therapy showed a 12.7% increase in NAA/Cr and (P= .03) in the multivoxel brain volume of interest (VOI) studied and by 9.6% (P= .04) in the normal-appearing white matter within the VOI. Three patients in the control group who began therapy with GA during the course of the study showed similar increases in NAA/Cr after the first year of therapy. These data support the long-term effect of GA on maintaining axonal metabolic function and protection from sublethal injury as well as the feasibility of employing brain (1)H-MRS in long-term investigative studies in MS.

Knapik JJ, Marin RE, Grier TL, Jones BH (2009) A systematic review of post-deployment injury-related mortality among military personnel deployed to conflict zones. BMC Public Health 9:231-252.
Abstract: BACKGROUND: This paper reports on a systematic review of the literature on the post-conflict injury-related mortality of service members who deployed to conflict zones. METHODS: Literature databases, reference lists of articles, agencies, investigators, and other sources were examined to find studies comparing injury-related mortality of military veterans who had served in conflict zones with that of contemporary veterans who had not served in conflict zones. Injury-related mortality was defined as a cause of death indicated by International Classification of Diseases E-codes E800 to E999 (external causes) or subgroupings within this range of codes. RESULTS: Twenty studies met the review criteria; all involved veterans serving during either the Vietnam or Persian Gulf conflict. Meta-analysis indicated that, compared with non-conflict-zone veterans, injury-related mortality was elevated for veterans serving in Vietnam (summary mortality rate ratio (SMRR) = 1.26, 95% confidence interval (95%CI) = 1.08-1.46) during 9 to 18 years of follow-up. Similarly, injury-related mortality was elevated for veterans serving in the Persian Gulf War (SMRR = 1.26, 95%CI = 1.16-1.37) during 3 to 8 years of follow-up. Much of the excess mortality among conflict-zone veterans was associated with motor vehicle events. The excess mortality decreased over time. Hypotheses to account for the excess mortality in conflict-zone veterans included post-traumatic stress, coping behaviors such as substance abuse, ill-defined diseases and symptoms, lower survivability in injury events due to conflict-zone comorbidities, altered perceptions of risk, and/or selection processes leading to the deployment of individuals who were risk-takers. CONCLUSION: Further research on the etiology of the excess mortality in conflict-zone veterans is warranted to develop appropriate interventions.

Krupka KM, Parkhurst MA, Gold K, Arey BW, Jenson ED, Guilmette RA (2009) Physicochemical characterization of Capstone depleted uranium aerosols III: morphologic and chemical oxide analyses. Health Phys 96:276-291.
Abstract: The impact of depleted uranium (DU) penetrators against an armored target causes erosion and fragmentation of the penetrators, the extent of which is dependent on the thickness and material composition of the target. Vigorous oxidation of the DU particles and fragments creates an aerosol of DU oxide particles and DU particle agglomerations combined with target materials. Aerosols from the Capstone DU aerosol study, in which vehicles were perforated by DU penetrators, were evaluated for their oxidation states using x-ray diffraction (XRD), and particle morphologies were examined using scanning electron microscopy/energy dispersive spectroscopy (SEM/EDS). The oxidation state of a DU aerosol is important as it offers a clue to its solubility in lung fluids. The XRD analysis showed that the aerosols evaluated were a combination primarily of U3O8 (insoluble) and UO3 (relatively more soluble) phases, though intermediate phases resembling U4O9 and other oxides were prominent in some samples. Analysis of particle residues in the micrometer-size range by SEM/EDS provided microstructural information such as phase composition and distribution, fracture morphology, size distribution, and material homogeneity. Observations from SEM analysis show a wide variability in the shapes of the DU particles. Some of the larger particles were spherical, occasionally with dendritic or lobed surface structures. Others appear to have fractures that perhaps resulted from abrasion and comminution, or shear bands that developed from plastic deformation of the DU material. Amorphous conglomerates containing metals other than uranium were also common, especially with the smallest particle sizes. A few samples seemed to contain small bits of nearly pure uranium metal, which were verified by EDS to have a higher uranium

content exceeding that expected for uranium oxides. Results of the XRD and SEM/EDS analyses were used in other studies described in this issue of Health Physics to interpret the results of lung solubility studies and in selecting input parameters for dose assessments.

Lamproglou I, Barbier L, Diserbo M, Fauvelle F, Fauquette W, Amourette C (2009) Repeated stress in combination with pyridostigmine Part I: long-term behavioural consequences. Behav Brain Res 197:301-310.
Abstract: Since their return from the first Persian Gulf War, some veterans have complained of a variety of symptoms that were designated as "Gulf War Illness" (GWI). Among other factors, pyridostigmine, used as a prophylaxis treatment against intoxication by nerve agents, has been proposed by many authors as a cause of late social and/or cognitive dysfunction related to GWI. One of the hypotheses placed to explain these behavioural disorders is that operational stress has modified the side effects of pyridostigmine given to soldiers. In an attempt to establish an experimental model of GWI to evaluate the long-term behavioural effects of pyridostigmine administered in stressful conditions, we have developed a new model of repeated stress based on the pole-climbing avoidance technique. We used it to evaluate the effects of pyridostigmine treatment combined to repeated stress over the months following the end of the treatment. We observed that this stress induces impulsiveness and aggressiveness in adult male rat. Moreover, pyridostigmine treatment administered daily 30 min before each stressful session amplifies these behavioural disorders and induces long-term learning dysfunction and slight but significant decrease in phosphocholine level in hippocampus. This suggests that repeated administration of pyridostigmine combined to pole-climbing avoidance (PCA) stress conditions can induce adverse effects in rat central nervous system.

Lestaevel P, Romero E, Dhieux B, Ben SH, Berradi H, Dublineau I, Voisin P, Gourmelon P (2009) Different pattern of brain pro-/anti-oxidant activity between depleted and enriched uranium in chronically exposed rats. Toxicology 258:1-9.
Abstract: Uranium is not only a heavy metal but also an alpha particle emitter. The main toxicity of uranium is expected to be due to chemiotoxicity rather than to radiotoxicity. Some studies have demonstrated that uranium induced some neurological disturbances, but without clear explanations. A possible mechanism of this neurotoxicity could be the oxidative stress induced by reactive oxygen species imbalance. The aim of the present study was to determine whether a chronic ingestion of uranium induced anti-oxidative defence mechanisms in the brain of rats. Rats received depleted (DU) or 4% enriched (EU) uranyl nitrate in the drinking water at 2mg(-1)kg(-1)day(-1) for 9 months. Cerebral cortex analyses were made by measuring mRNA and protein levels and enzymatic activities. Lipid peroxidation, an oxidative stress marker, was significantly enhanced after EU exposure, but not after DU. The gene expression or activity of the main antioxidant enzymes, i.e. superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), increased significantly after chronic exposure to DU. On the contrary, oral EU administration induced a decrease of these antioxidant enzymes. The NO-ergic pathway was almost not perturbed by DU or EU exposure. Finally, DU exposure increased significantly the transporters (Divalent-Metal-Transporter1; DMT1), the storage molecule (ferritin) and the ferroxidase enzyme (ceruloplasmin), but not EU. These results illustrate that oxidative stress plays a key role in the mechanism of uranium neurotoxicity. They showed that chronic exposure to DU, but not EU, seems to induce an increase of several antioxidant agents in order to counteract the oxidative stress. Finally, these results demonstrate the importance of the double toxicity, chemical and radiological, of uranium.

Li WB, Gerstmann UC, Hollriegl V, Szymczak W, Roth P, Hoeschen C, Oeh U (2009) Radiation dose assessment of exposure to depleted uranium. J Expo Sci Environ Epidemiol 19:502-514.
Abstract: 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 x 10(-8) and 2.1 x 10(-6) Sv Bq(-1) 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.

Lind OC, Salbu B, Skipperud L, Janssens K, Jaroszewicz J, De NW (2009) Solid state speciation and potential bioavailability of depleted uranium particles from Kosovo and Kuwait. J Environ Radioact 100:301-307.
Abstract: A combination of synchrotron radiation based X-ray microscopic techniques (mu-XRF, mu-XANES, mu-XRD) applied on single depleted uranium (DU) particles and semi-bulk leaching experiments has been employed to link the potential bioavailability of DU particles to site-specific particle characteristics. The oxidation states and crystallographic forms of U in DU particles have been determined for individual particles isolated from selected samples collected at different sites in Kosovo and Kuwait that were contaminated by DU ammunition during the 1999 Balkan conflict and the 1991 Gulf war. Furthermore, small soil or sand samples heavily contaminated with DU particles were subjected to simulated gastrointestinal fluid (0.16 M HCl) extractions. Characteristics of DU particles in Kosovo soils collected in 2000 and in Kuwait soils collected in 2002 varied significantly depending on the release scenario and to some extent on weathering conditions. Oxidized U (+6) was determined in large, fragile and bright yellow DU particles released during fire at a DU ammunition storage facility and crystalline phases such as schoepite (UO(3).2.25H(2)O), dehydrated schoepite (UO(3).0.75H(2)O) and metaschoepite (UO(3).2.0H(2)O) were identified. As expected, these DU particles were rapidly dissolved in 0.16 M HCl (84 +/- 3% extracted after 2 h) indicating a high degree of potential mobility and bioavailability. In contrast, the 2 h extraction of samples contaminated with DU particles originating either from corrosion of unspent DU penetrators or from impacted DU ammunition appeared to be much slower (20-30%) as uranium was less oxidized (+4 to +6). Crystalline phases such as UO(2), UC and metallic U or U-Ti alloy were determined in impacted DU particles from Kosovo and Kuwait, while the UO(2,34) phase, only determined in particles from Kosovo, could reflect a more corrosive environment. Although the results are based on a limited number of DU particles, they indicate that the structure and extractability of DU particles released from similar sources (metallic U penetrators) will depend on the release scenarios (fire, impact) and to some extent environmental conditions. However, most of the DU particles (73-96%) in all investigated samples were dissolved in 0.16 M HCl after one week indicating that a majority of the DU material is bioaccessible.

Maes M, Mihaylova I, Kubera M, Uytterhoeven M, Vrydags N, Bosmans E (2009) Increased 8-hydroxy-deoxyguanosine, a marker of oxidative damage to DNA, in major depression and myalgic encephalomyelitis / chronic fatigue syndrome. Neuro Endocrinol Lett 30.
Abstract: There is now evidence that major depression and myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) are accompanied by partially overlapping pathophysiological mechanisms, i.e. activation of various inflammatory and oxidative & nitrosative (IO&NS) pathways. The aim of the present study was to examine the urinary excretion of 8-hydroxy-deoxyguanosine (8-OhdG), a marker of oxidative damage to DNA, in depression; ME/CFS; and depression and ME/CFS. Toward this end, morning urine was sampled for the assays of 8-OHdG and creatinine, in 44 patients with ME/CFS; 25 with major depression; 23 with depression and ME/CFS; and 17 normal controls. Severity of fatigue and somatic symptoms was measured by means of the Fibromyalgia and CFS Rating (FF) scale. We found that 49.0% of the variance in the urinary excretion of 8-OHdG was predicted by the regression on creatinine. Consequently, the urinary 8-OHdG excretion should be expressed as the residualized 8-OHdG values after partialling out the effects of creatinine and not by computing the 8-OHdG / creatinine ratio. We found that the residualized urinary excretion of 8-OHdG (adjusted for creatinine) was significantly higher in patients with depression and ME/CFS than in normal controls and all other patients. In the patient group, there were significant correlations between the urinary 8-OHdG and the total score on the FF scale and sadness and flu-like malaise. The findings show increased oxidatively generated DNA damage in patients with major depression and ME/CFS and, therefore, further extent the role played by IO&NS pathways in the pathophysiology of both disorders. Since oxidatively damage to DNA is a risk factor for atherosclerosis and neurodegeneration, our results also explain previous findings on increased cardiovascular morbidity in depression and ME/CFS, and neurodegenerative processes in depression.

McDiarmid MA, Engelhardt SM, Dorsey CD, Oliver M, Gucer P, Wilson PD, Kane R, Cernich A, Kaup B, Anderson L, Hoover D, Brown L, Albertini R, Gudi R, Squibb KS (2009) Surveillance results of depleted uranium-exposed Gulf War I veterans: sixteen years of follow-up. J Toxicol Environ Health A 72:14-29.
Abstract: As part of a longitudinal surveillance program, 35 members of a larger cohort of 77 Gulf War I veterans who were victims of depleted uranium (DU) "friendly fire" during combat underwent a 3-day clinical assessment at the Baltimore Veterans Administration Medical Center (VAMC). The assessment included a detailed medical history, exposure history, physical examination, and laboratory studies. Spot and 24-h urine collections were obtained for renal function parameters and for urine uranium (U) measures. Blood U measures were also performed. Urine U excretion was significantly associated with DU retained shrapnel burden (8.821 mug U/g creatinine [creat.] vs. 0.005 mug U/g creat., p = .04). Blood as a U sampling matrix revealed satisfactory results for measures of total U with a high correlation with urine U results (r = .84) when urine U concentrations were >/=0.1 mug/g creatinine. However, isotopic results in blood detected DU in only half of the subcohort who had isotopic signatures for DU detectable in urine. After

stratifying the cohort based on urine U concentration, the high-U group showed a trend toward higher concentrations of urine beta(2) microglobulin compared to the low-U group (81.7 v. 69.0 mug/g creat.; p = .11 respectively) and retinol binding protein (48.1 vs. 31.0 mug/g creat.; p = .07 respectively). Bone metabolism parameters showed only subtle differences between groups. Sixteen years after first exposure, this cohort continues to excrete elevated concentrations of urine U as a function of DU shrapnel burden. Although subtle trends emerge in renal proximal tubular function and bone formation, the cohort exhibits few clinically significant U-related health effects.

McKenzie DP, Creamer M, Kelsall HL, Forbes AB, Ikin JF, Sim MR, McFarlane AC (2009) Temporal relationships between Gulf War deployment and subsequent psychological disorders in Royal Australian Navy Gulf War veterans. Soc Psychiatry Psychiatr Epidemiol.
Abstract: BACKGROUND: Although much has been published on the effects of the 1990/1991 Gulf War on the psychological health of veterans, few studies have addressed the pattern and timing of post-war development of psychological disorders. Our study aims to identify the most common psychological disorders that first appeared post-Gulf War, the period of peak prevalence and the sequence of multiple psychological disorders. METHODS: The temporal progression of psychological disorders in male Australian naval Gulf War veterans with no prior psychological disorders was calculated across each year of the post-Gulf War period. DSM-IV diagnoses were obtained using the Composite International Diagnostic Interview. RESULTS: Psychological disorder rates peaked in the first 2 years (1991-1992) following the Gulf War. Alcohol use disorders were the most likely to appear first. Classification and regression tree analysis found that risk of disorder was exacerbated if veterans had been exposed to a high number of potential psychological stressors during their military service. Lower military rank was associated with increased risk of alcohol disorders, particularly during the first 2 years post-Gulf War. In veterans with two or more disorders, anxiety disorders and alcohol disorders tended to appear before affective disorders. CONCLUSIONS: Our study found that psychological disorders occur in sequence following Gulf War deployment. Our findings may help clinicians to anticipate, and better manage, multiple symptomatology. The findings may also assist veteran and defence organisations in planning effective mental health screening, management and prevention policy.

Miller G, Cheng YS, Traub RJ, Little TT, Guilmette RA (2009) Methods used to calculate doses resulting from inhalation of Capstone depleted uranium aerosols. Health Phys 96:306-327.
Abstract: The methods used to calculate radiological and toxicological doses to hypothetical persons inside either a U.S. Army Abrams tank or Bradley Fighting Vehicle that has been perforated by depleted uranium munitions are described. Data from time- and particle-size-resolved measurements of depleted uranium aerosol as well as particle-size-resolved measurements of aerosol solubility in lung fluids for aerosol produced in the breathing zones of the hypothetical occupants were used. The aerosol was approximated as a mixture of nine monodisperse (single particle size) components corresponding to particle size increments measured by the eight stages plus the backup filter of the cascade impactors used. A Markov Chain Monte Carlo Bayesian analysis technique was employed, which straightforwardly calculates the uncertainties in doses. Extensive quality control checking of the various computer codes used is described.

Myhill S, Booth NE, Laren-Howard J (2009) Chronic fatigue syndrome and mitochondrial dysfunction. Int J Clin Exp Med 2:1-16.
Abstract: This study aims to improve the health of patients suffering from chronic fatigue syndrome (CFS) by interventions based on the biochemistry of the illness, specifically the function of mitochondria in producing ATP (adenosine triphosphate), the energy currency for all body functions, and recycling ADP (adenosine diphosphate) to replenish the ATP supply as needed. Patients attending a private medical practice specializing in CFS were diagnosed using the Centers for Disease Control criteria. In consultation with each patient, an integer on the Bell Ability Scale was assigned, and a blood sample was taken for the "ATP profile" test, designed for CFS and other fatigue conditions. Each test produced 5 numerical factors which describe the availability of ATP in neutrophils, the fraction complexed with magnesium, the efficiency of oxidative phosphorylation, and the transfer efficiencies of ADP into the mitochondria and ATP into the cytosol where the energy is used. With the consent of each of 71 patients and 53 normal, healthy controls the 5 factors have been collated and compared with the Bell Ability Scale. The individual numerical factors show that patients have different combinations of biochemical lesions. When the factors are combined, a remarkable correlation is observed between the degree of mitochondrial dysfunction and the severity of illness ($P<0.001$). Only 1 of the 71 patients overlaps the normal region. The "ATP profile" test is a powerful diagnostic tool and can differentiate patients who have fatigue and other symptoms as a result of energy wastage by stress and psychological factors from those who have insufficient energy due to cellular respiration dysfunction. The individual factors indicate which remedial actions, in the form of dietary supplements, drugs and detoxification, are most likely to be of benefit, and what further tests should be carried out.

Parkhurst MA, Cheng YS, Kenoyer JL, Traub RJ (2009) Physicochemical characterization of Capstone depleted uranium aerosols I: uranium concentration in aerosols as a function of time and particle size. Health Phys 96:251-265.

Abstract: During the Capstone Depleted Uranium (DU) Aerosol Study, aerosols containing DU were produced inside unventilated armored vehicles (i.e., Abrams tanks and Bradley Fighting Vehicles) by perforation with large-caliber DU penetrators. These aerosols were collected and characterized, and the data were subsequently used to assess human health risks to personnel exposed to DU aerosols. The DU content of each aerosol sample was first quantified by radioanalytical methods, and selected samples, primarily those from the cyclone separator grit chambers, were analyzed radiochemically. Deposition occurred inside the vehicles as particles settled on interior surfaces. Settling rates of uranium from the aerosols were evaluated using filter cassette samples that collected aerosol as total mass over eight sequential time intervals. A moving filter was used to collect aerosol samples over time, particularly within the first minute after a shot. The results demonstrate that the peak uranium concentration in the aerosol occurred in the first 10 s after perforation, and the concentration decreased in the Abrams tank shots to about 50% within 1 min and to less than 2% after 30 min. The initial and maximum uranium concentrations were lower in the Bradley vehicle than those observed in the Abrams tank, and the concentration levels decreased more slowly. Uranium mass concentrations in the aerosols as a function of particle size were evaluated using samples collected in a cyclone sampler, which collected aerosol continuously for 2 h after perforation. The percentages of uranium mass in the cyclone separator stages ranged from 38 to 72% for the Abrams tank with conventional armor. In most cases, it varied with particle size, typically with less uranium associated with the smaller particle sizes. Neither the Abrams tank with DU armor nor the Bradley vehicle results were specifically correlated with particle size and can best be represented by their average uranium mass concentrations of 65 and 24%, respectively.

Parkhurst MA, Guilmette RA (2009a) Overview of the Capstone depleted uranium study of aerosols from impact with armored vehicles: test setup and aerosol generation, characterization, and application in assessing dose and risk. Health Phys 96:207-220.

Abstract: The Capstone Depleted Uranium (DU) Aerosol Characterization and Risk Assessment Study was conducted to generate data about DU aerosols generated during the perforation of armored combat vehicles with large-caliber DU penetrators, and to apply the data in assessments of human health risks to personnel exposed to these aerosols, primarily through inhalation, during the 1991 Gulf War or in future military operations. The Capstone study consisted of two components: 1) generating, sampling, and characterizing DU aerosols by firing at and perforating combat vehicles, and 2) applying the source-term quantities and characteristics of the aerosols to the evaluation of doses and risks. This paper reviews the background of the study including the bases for the study, previous reviews of DU particles and health assessments from DU used by the U.S. military, the objectives of the study components, the participants and oversight teams, and the types of exposures it was intended to evaluate. It then discusses exposure scenarios used in the dose and risk assessment and provides an overview of how the field tests and dose and risk assessments were conducted.

Parkhurst MA, Guilmette RA (2009b) Conclusions of the Capstone depleted uranium aerosol characterization and risk assessment study. Health Phys 96:393-409.

Abstract: The rationale for the Capstone Depleted Uranium (DU) Aerosol Characterization and Risk Assessment Study and its results and applications have been examined in the previous 13 articles of this special issue. This paper summarizes the study's results and discusses its successes and lessons learned. The robust data from the Capstone DU Aerosol Study have provided a sound basis for assessing the inhalation exposure to DU aerosols and the dose and risk to personnel in combat vehicles at the time of perforation and to those entering immediately after perforation. The Human Health Risk Assessment provided a technically sound process for evaluating chemical and radiological doses and risks from DU aerosol exposure using well-accepted biokinetic and dosimetric models innovatively applied. An independent review of the study process and results is summarized, and recommendations for possible avenues of future study are provided by the authors and by other major reviews of DU health hazards.

Pastula DM, Coffman CJ, Allen KD, Oddone EZ, Kasarskis EJ, Lindquist JH, Morgenlander JC, Norman BB, Rozear MP, Sams LA, Sabet A, Bedlack RS (2009) Factors associated with survival in the National Registry of Veterans with ALS. Amyotroph Lateral Scler 10:332-338.

Abstract: 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.

Rice NE, Bandinelli S, Corsi AM, Ferrucci L, Guralnik JM, Miller MA, Kumari M, Murray A, Frayling TM, Melzer D (2009) The paraoxonase (PON1) Q192R polymorphism is not associated with poor health status or depression in the ELSA or INCHIANTI studies. Int J Epidemiol 38:1374-1379.

Abstract: BACKGROUND: The human paraoxonase (PON1) protein detoxifies certain organophosphates, and the PON1 Q192R polymorphism (rs662) affects PON1 activity. Groups with higher dose exposure to organophosphate sheep dips or first Gulf War nerve toxins reported poorer health if they had 192R, and these associations have been used to exemplify Mendelian randomization analysis. However, a reported association of 192R with depression in a population-based study of older women recently cast doubt on the specificity of the higher dose findings. We aimed to examine associations between the PON1 Q192R polymorphism and self-reported poor health and depression in two independent population-based studies. METHODS: We used logistic regression models to examine the associations in men and women aged 60-79 years from the English Longitudinal Study of Ageing (ELSA, n = 3158) and InCHIANTI (n = 761) population studies. Outcomes included the Center for Epidemiologic Studies Depression (CES-D) scale, self-rated general health status and (in ELSA only) diagnoses of depression. RESULTS: The PON1 Q192R polymorphism was not associated with self-reported poor health {meta-analysis: odds ratio (OR) = 1.01 [confidence interval (CI) 0.91-1.13], P = 0.80} or depressive symptoms in either study or in meta-analyses [CES-D: OR = 1.01 (CI 0.87-1.17), P = 0.90]. There was also no association with histories of diagnosed depression in ELSA [OR = 1.03 (CI 0.82-1.30), P = 0.80]. CONCLUSIONS: We found no evidence of an association between the PON1 Q192R polymorphism and poor general or mental health in two independent population-based studies. Neither the claimed Q192R association with depression in the general population nor its theoretical implications were supported.

Rossbach B, Appel KE, Mross KG, Letzel S (2009) Uptake of permethrin from impregnated clothing. Toxicol Lett.

Abstract: In order to examine exposure and health risks which can arise from permethrin-impregnated clothing, a controlled trial was conducted. In a study group consisting of 187 volunteers in total, a subgroup of 86 persons was equipped with permethrin-impregnated battle dress uniforms (BDU) for 28 days. One hundred and one persons served as a control group, wearing non-impregnated BDUs throughout the entire study period of 56 days. Internal exposure of all participants was assessed by determination of urinary permethrin metabolites (cis-DCCA, trans-DCCA and 3-PBA) on day 0, 14 and 28 of the wearing period and 28 days after termination of wearing. Exposure levels in the control group ranged within background exposure of the general German population at all four dates of sampling (medians Σ DCCA+3-PBA were 0.09, 0.13, 0.23 and 0.10μg/l, respectively). For the group equipped with impregnated BDUs this applied to day 0 (0.31μg/l) only, while the following measurements revealed considerably higher metabolite concentrations (31.39, 22.01 and 1.44μg/l, respectively), especially while wearing impregnated clothing. Due to these results a substantial uptake of permethrin from impregnated BDUs has to be assumed. However, since calculations reveal a maximum permethrin uptake clearly below the acceptable daily intake (ADI), health impairments are rather unlikely.

Roszell LE, Hahn FF, Lee RB, Parkhurst MA (2009) Assessing the renal toxicity of Capstone depleted uranium oxides and other uranium compounds. Health Phys 96:343-351.

Abstract: The primary target for uranium toxicity is the kidney. The most frequently used guideline for uranium kidney burdens is the International Commission on Radiological Protection value of 3 μg U g^{-1} kidney, a value that is based largely upon chronic studies in animals. In the present effort, a risk model equation was developed to assess potential outcomes of acute uranium exposure. Twenty-seven previously published case studies in which workers were acutely exposed to soluble compounds of uranium (as a result of workplace accidents) were analyzed. Kidney burdens of uranium for these individuals were determined based on uranium in the urine, and correlated with health effects

observed over a period of up to 38 years. Based upon the severity of health effects, each individual was assigned a score (- to +++) and then placed into a Renal Effects Group (REG). A discriminant analysis was used to build a model equation to predict the REG based on the amount of uranium in the kidneys. The model equation was able to predict the REG with 85% accuracy. The risk model was used to predict the REG for soldiers exposed to depleted uranium as a result of friendly fire incidents during the 1991 Gulf War. This model equation can also be used to predict the REG of new cases in which acute exposures to uranium have occurred.

Shaw CA, Petrik MS (2009) Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration. J Inorg Biochem 103:1555-1562.

Abstract: Gulf War Syndrome is a multi-system disorder afflicting many veterans of Western armies in the 1990-1991 Gulf War. A number of those afflicted may show neurological deficits including various cognitive dysfunctions and motor neuron disease, the latter expression virtually indistinguishable from classical amyotrophic lateral sclerosis (ALS) except for the age of onset. This ALS "cluster" represents the second such ALS cluster described in the literature to date. Possible causes of GWS include several of the adjuvants in the anthrax vaccine and others. The most likely culprit appears to be aluminum hydroxide. In an initial series of experiments, we examined the potential toxicity of aluminum hydroxide in male, outbred CD-1 mice injected subcutaneously in two equivalent-to-human doses. After sacrifice, spinal cord and motor cortex samples were examined by immunohistochemistry. Aluminum-treated mice showed significantly increased apoptosis of motor neurons and increases in reactive astrocytes and microglial proliferation within the spinal cord and cortex. Morin stain detected the presence of aluminum in the cytoplasm of motor neurons with some neurons also testing positive for the presence of hyper-phosphorylated tau protein, a pathological hallmark of various neurological diseases, including Alzheimer's disease and frontotemporal dementia. A second series of experiments was conducted on mice injected with six doses of aluminum hydroxide. Behavioural analyses in these mice revealed significant impairments in a number of motor functions as well as diminished spatial memory capacity. The demonstrated neurotoxicity of aluminum hydroxide and its relative ubiquity as an adjuvant suggest that greater scrutiny by the scientific community is warranted.

Smith-Osborne A (2009) Mental Health Risk and Social Ecological Variables Associated with Educational Attainment for Gulf War Veterans: Implications for Veterans Returning to Civilian Life. Am J Community Psychol.

Abstract: This study examines how post-secondary educational attainment among young veterans of the first gulf war affects their mental health status. The all-volunteer military attracts recruits by offering them veterans' educational benefits. Education should help veterans adjust to civilian life. Few studies have shown whether education following military service helps improve veterans' mental health, however. Viewing resiliency, life span and life course, and social geography theories through the lens of social ecology, it is hypothesized that selected contextual factors in the personal, interpersonal, and organizational domains could mediate or moderate the relationship between education and veterans' mental health. Informational social networks showed an association with obtaining mental illness treatment. Recent treatment for post-traumatic stress disorder (PTSD) showed an association with use of veterans' educational benefits. Residing with a small nuclear family in conjunction with having higher levels of health and educational benefits and a higher family income was associated with higher educational attainment.

Sutedja NA, Veldink JH, Fischer K, Kromhout H, Heederik D, Huisman MH, Wokke JH, van den Berg LH (2009) Exposure to chemicals and metals and risk of amyotrophic lateral sclerosis: a systematic review. Amyotroph Lateral Scler 10:302-309.

Abstract: Environmental exposure to chemicals and metals may contribute to the risk of sporadic amyotrophic lateral sclerosis (ALS). Two systematic reviews of the literature on these topics performed according to the well-established MOOSE guidelines are presented. Literature cited in MEDLINE, EMBASE, CINAHL, and Cochrane databases (up to March 2007) as well as references of relevant articles were screened for case-control or cohort studies investigating the associations between sporadic ALS and exposure to chemical agents or metals. Methodology of selected studies was appraised according to Armon's classification system for ALS risk factor studies as well as a newly developed classification system for quality of exposure assessment. Seven of the 38 studies concerning exposure to chemicals and three of the 50 studies concerning exposure to metals fulfilled the validity criteria. In two independent studies meeting the validity criteria, a significant association with increased ALS risk was reported for exposure to pesticides. This systematic review demonstrated the difficulty in attaining a high level of evidence due to lack of high quality of methodological and exposure assessment components. Although pesticide exposure was identified as candidate risk factor, more well-designed studies are needed to provide a definitive answer about exogenous factors of ALS.

Szrom F, Falo GA, Lodde GM, Parkhurst MA, Daxon EG (2009) Inhalation and ingestion intakes with associated dose estimates for level II and level III personnel using Capstone study data. Health Phys 96:363-379.
Abstract: Depleted uranium (DU) intake rates and subsequent dose rates were estimated for personnel entering armored combat vehicles perforated with DU penetrators (level II and level III personnel) using data generated during the Capstone DU Aerosol Study. Inhalation intake rates and associated dose rates were estimated from cascade impactors worn by sample recovery personnel and from cascade impactors that served as area monitors. Ingestion intake rates and associated dose rates were estimated from cotton gloves worn by sample recovery personnel and from wipe-tests samples from the interior of vehicles perforated with large-caliber DU munitions. The mean DU inhalation intake rate for level II personnel ranged from 0.447 mg h^{-1} based on breathing zone monitor data (in and around a perforated vehicle) to 14.5 mg h^{-1} based on area monitor data (in a perforated vehicle). The mean DU ingestion intake rate for level II ranged from 4.8 mg h^{-1} to 38.9 mg h^{-1} based on the wipe-tests data including surface-to-glove transfer factors derived from the Capstone data. Based on glove contamination data, the mean DU ingestion intake rates for level II and level III personnel were 10.6 mg h^{-1} and 1.78 mg h^{-1}, respectively. Effective dose rates and peak kidney uranium concentration rates were calculated based on the intake rates. The peak kidney uranium concentration rate cannot be multiplied by the total exposure duration when multiple intakes occur because uranium will clear from the kidney between the exposures.

Toomey R, Alpern R, Vasterling JJ, Baker DG, Reda DJ, Lyons MJ, Henderson WG, Kang HK, Eisen SA, Murphy FM (2009) Neuropsychological functioning of U.S. Gulf War veterans 10 years after the war. J Int Neuropsychol Soc 15:717-729.
Abstract: Many U.S. Gulf War-era veterans complained of poor cognition following the war. This study assessed neuropsychological functioning in veterans 10 years after the war through objective tests. 2189 Gulf War-era veterans (1061 deployed, 1128 non-deployed) were examined at 1 of 16 U.S. Veterans Affairs medical centers. Outcomes included neuropsychological domains derived from factor analysis and individual test scores. Deployed veterans performed significantly worse than non-deployed veterans on 2 of 8 factors (motor speed & sustained attention, analysis not corrected for multiple comparisons) and on 4 of 27 individual test variables (Trails A & B, California Verbal Learning Test-List B, and Continuous Performance Test sensitivity, with only Trails B surviving Bonferroni correction). Within deployed veterans, Khamisiyah exposure was negatively correlated with motor speed after controlling for emotional distress. Depressive symptoms and self-reported exposure to toxicants were independently and significantly associated with worse sustained attention. Other factors were also associated with self-reported exposures. The findings were not a result of differential effort across groups. Gulf War deployment is associated with subtle declines of motor speed and sustained attention, despite overall intact neuropsychological functioning. Evidence suggests that toxicant exposures influence both these functions, and depressive symptoms also influence attention.

Wallin MT, Wilken J, Alfaro MH, Rogers C, Mahan C, Chapman JC, Fratto T, Sullivan C, Kang H, Kane R (2009) Neuropsychologic assessment of a population-based sample of Gulf War veterans. Cogn Behav Neurol 22:155-166.
Abstract: OBJECTIVE: The objective of this project was to compare neuropsychologic performance and quality of life in a population-based sample of deployed Gulf War (GW) veterans with and without multisymptom complaints. BACKGROUND/METHODS: The study participants were obtained from the 30,000 member population-based National Health Survey of GW-era veterans conducted in 1995. Cases (N=25) were deployed to the year 1990 and 1991 GW and met Center for Disease Control and Prevention criteria for multisymptom GW illness (GWI). Controls (N=16) were deployed to the 1990 and 1991 GW but did not meet Center for Disease Control and Prevention criteria for GWI. RESULTS: There were no significant differences in composite scores on the traditional and computerized neuropsychologic battery (automated neuropsychologic assessment metrics) between GW cases and controls using bivariate techniques. Multiple linear regression analyses controlling for demographic and clinical variables revealed composite automated neuropsychologic assessment metrics scores were associated with age (b=-7.8; P=0.084), and education (b=22.9; P=0.0012), but not GW case or control status (b=-63.9; P=0.22). Compared with controls, GW cases had significantly more impairment on the Personality Assessment Inventory and the short form-36. CONCLUSIONS: Compared with GW controls, GW cases meeting criteria for GWI had preserved cognition function but had significant psychiatric symptoms and lower quality of life.

Ware MA, Fitzcharles MA, Joseph L, Shir Y (2009) The Effects of Nabilone on Sleep in Fibromyalgia: Results of a Randomized Controlled Trial. Anesth Analg.

Abstract: Background: Sleep disorders affect many patients with chronic pain conditions. Cannabis has been reported by several patient populations to help sleep. We evaluated the safety and efficacy of nabilone, a synthetic cannabinoid, on sleep disturbance in fibromyalgia (FM), a disease characterized by widespread chronic pain and insomnia. Methods: We conducted a randomized, double-blind, active-control, equivalency crossover trial to compare nabilone (0.5-1.0 mg

before bedtime) to amitriptyline (10-20 mg before bedtime) in patients with FM with chronic insomnia. Subjects received each drug for 2 wk with a 2-wk washout period. The primary outcome was sleep quality, measured by the Insomnia Severity Index and the Leeds Sleep Evaluation Questionnaire. Secondary outcomes included pain, mood, quality of life, and adverse events (AEs). Results: Thirty-one subjects were enrolled and 29 completed the trial (26 women, mean age 49.5 yr). Although sleep was improved by both amitriptyline and nabilone, nabilone was superior to amitriptyline (Insomnia Severity Index difference = 3.2; 95% confidence interval = 1.2-5.3). Nabilone was marginally better on the restfulness (Leeds Sleep Evaluation Questionnaire difference = 0.5 [0.0-1.0]) but not on wakefulness (difference = 0.3 [-0.2 to 0.8]). No effects on pain, mood, or quality of life were observed. AEs were mostly mild to moderate and were more frequent with nabilone. The most common AEs for nabilone were dizziness, nausea, and dry mouth. Conclusions: Nabilone is effective in improving sleep in patients with FM and is well tolerated. Low-dose nabilone given once daily at bedtime may be considered as an alternative to amitriptyline. Longer trials are needed to determine the duration of effect and to characterize long-term safety.

Whistler T, Fletcher MA, Lonergan W, Zeng XR, Lin JM, Laperriere A, Vernon SD, Klimas NG (2009) Impaired immune function in Gulf War Illness. BMC Med Genomics 2:12.
Abstract: BACKGROUND: Gulf War Illness (GWI) remains a serious health consequence for at least 11,000 veterans of the first Gulf War in the early 1990s. Our understanding of the health consequences that resulted remains inadequate, and this is of great concern with another deployment to the same theater of operations occurring now. Chronic immune cell dysfunction and activation have been demonstrated in patients with GWI, although the literature is not uniform. We exposed GWI patients and matched controls to an exercise challenge to explore differences in immune cell function measured by classic immune assays and gene expression profiling. METHODS: This pilot study enrolled 9 GWI cases identified from the Department of Veterans Affairs GWI registry, and 11 sedentary control veterans who had not been deployed to the Persian Gulf and were matched to cases by sex, body mass index (BMI) and age. We measured peripheral blood cell numbers, NK cytotoxicity, cytokines and expression levels of 20,000 genes immediately before, immediately after and 4 hours following a standard bicycle ergometer exercise challenge. RESULTS: A repeated-measures analysis of variance revealed statistically significant differences for three NK cell subsets and NK cytotoxicity between cases and controls ($p < 0.05$). Linear regression analysis correlating NK cell numbers to the gene expression profiles showed high correlation of genes associated with NK cell function, serving as a biologic validation of both the in vitro assays and the microarray platform. Intracellular perforin levels in NK and CD8 T-cells trended lower and showed a flatter profile in GWI cases than controls, as did the expression levels of the perforin gene PRF1. Genes distinguishing cases from controls were associated with the glucocorticoid signaling pathway. CONCLUSION: GWI patients demonstrated impaired immune function as demonstrated by decreased NK cytotoxicity and altered gene expression associated with NK cell function. Pro-inflammatory cytokines, T-cell ratios, and dysregulated mediators of the stress response (including salivary cortisol) were also altered in GWI cases compared to control subjects. An interesting and potentially important observation was that the exercise challenge augments these differences, with the most significant effects observed immediately after the stressor, possibly implicating some block in the NK and CD8 T-cells ability to respond to "stress-mediated activation". This has positive implications for the development of laboratory diagnostic tests for this syndrome and provides a paradigm for exploration of the immuno-physiological mechanisms that are operating in GWI, and similar complex syndromes. Our results do not necessarily elucidate the cause of GWI, but they do reveal a role for immune cell dysfunction in sustaining illness.

Woodward SH, Kaloupek DG, Grande LJ, Stegman WK, Kutter CJ, Leskin L, Prestel R, Schaer M, Reiss AL, Eliez S (2009a) Hippocampal volume and declarative memory function in combat-related PTSD. J Int Neuropsychol Soc 15:830-839 (Epub 2009 Aug 25).
Abstract: The proposition that declarative memory deficits are systematically related to smaller hippocampal volume was tested in a relatively large sample (n = 95) of U.S. military veterans with and without combat-related posttraumatic stress disorder. This correlative analysis was extended by including multiple measures of verbal and visual declarative memory and multiple memory-relevant regional brain volumes that had been shown to exhibit main effects of PTSD in prior work. Small-to-moderate effects were observed on verbal declarative memory in line with a recent meta-analysis; nevertheless, little or no evidence of systematic linear covariation between memory measures and brain volumes was observed

Woodward SH, Schaer M, Kaloupek DG, Cediel L, Eliez S (2009b) Smaller global and regional cortical volume in combat-related posttraumatic stress disorder. Arch Gen Psychiatry 66:1373-1382.
Abstract: CONTEXT: Two sets of findings predict smaller cerebral cortical gray matter volume in adult posttraumatic stress disorder (PTSD). Measures of intracranial tissue volume and cerebral tissue volume have been observed to be smaller in adolescents with maltreatment-related PTSD. Second, lower intelligence, a risk factor for PTSD, is associated

with smaller cerebral tissue volumes. Nevertheless, to our knowledge, only 1 study has observed globally smaller cerebral tissue volume in adults with PTSD. OBJECTIVES: To apply a recently developed method providing improved estimates of cortical volume and to estimate associations between adult PTSD and selected regional cortical volumes not yet investigated. DESIGN: Between-group comparison of global and regional cerebral cortical volumes in adult patients with combat-related PTSD and controls. SETTING: Two Department of Veterans Affairs medical centers with large inpatient and outpatient PTSD catchments. PARTICIPANTS: Ninety-seven combat-exposed veterans of the Vietnam and Persian Gulf wars. MAIN OUTCOME MEASURE: Global and regional cortical volumes determined using the FreeSurfer software program and the Desikan et al parcellation (modified). RESULTS: Cerebral cortical volume, thickness, and area were observed to be smaller in association with adult combat-related PTSD. Robust associations were observed between PTSD and smaller cortical volumes in the parahippocampal gyrus, superior temporal cortex, lateral orbital frontal cortex, and pars orbitalis of the inferior frontal gyrus. CONCLUSIONS: Cerebral cortical volume, thickness, and area may be smaller in adult chronic severe PTSD; however, the extracted structural variables did not mediate relations between intelligence and PTSD. The 4 regions exhibiting especially smaller cortical volumes in this sample share involvement in mechanisms subserving "top-down" facilitation of the identification of objects and words. Compromise of these regions may result in difficulty in relearning pretrauma schemata for interpreting the civilian physical and social environments.

Xie H, Lacerte C, Thompson WD, Wise JP (2009) Depleted Uranium Induces Neoplastic Transformation in Human Lung Epithelial Cells. Chem Res Toxicol.
Abstract: Depleted uranium (DU) is commonly used in military armor and munitions, and thus, exposure of soldiers and noncombatants is frequent and widespread. Previous studies have shown that DU has both chemical and radiological toxicity and that the primary route of exposure of DU to humans is through inhalation and ingestion. However, there is limited research information on the potential carcinogenicity of DU in human bronchial cells. Accordingly, we determined the neoplastic transforming ability of particulate DU to human bronchial epithelial cells (BEP2D). We observed the loss of contact inhibition and anchorage independent growth in cells exposed to DU after 24 h. We also characterized these DU-induced transformed cell lines and found that 40% of the cell lines exhibit alterations in plating efficiency and no significant changes in the cytotoxic response to DU. Cytogenetic analyses showed that 53% of the DU-transformed cell lines possess a hypodiploid phenotype. These data indicate that human bronchial cells are transformed by DU and exhibit significant chromosome instability consistent with a neoplastic phenotype.

Young, HA, Maillard, JD, Levine, PH, Simmens, SJ, Mahan, CM, Kang, HK (2009) Assessing risk of cancer in Gulf War veterans using state cancer registry data. Annals of Epidemiology 19:654
Abstract: PURPOSE: The purpose of this study was to determine whether proportional cancer incidence is greater among Gulf War veterans compared with non-Gulf War veterans. METHODS: Files obtained from the Defense Manpower Data Center included data for 621,902 veterans who were deployed to the Persian Gulf during the 1990 to 1991 Gulf War (August 2, 1990, to March 1, 1991) and 746,248 non-Gulf War veteran controls. Identification of veterans who received a cancer diagnosis between 1991 and 2006 was accomplished through record linkage of the Defense Manpower Data Center dataset with files from 28 state cancer registries and the Department of Veterans Affairs Central Cancer Registry. By the use of logistic regression, proportional incidence ratios adjusted for demographic and military characteristics were calculated by comparing the proportion of a specific cancer among all cancers in the Gulf War veterans to the proportion of that specific cancer among all cancers in the non-Gulf War veterans. RESULTS: Only lung cancer showed a statistically significant relative excess among Gulf War veterans compared with non-Gulf War veterans (adjusted proportional incidence ratios, 1.15; 95% confidence interval, 1.03-1.29). When adjusted for race, age, and sex, the overall proportion of cancers among Gulf War and non-Gulf War veterans was similar (odds ratio, 0.99; 95% CI, 0.96-1.02). CONCLUSIONS: With the exception of lung cancer, there is little evidence of excess risk of cancer associated with Gulf War deployment. A follow-up study is warranted to confirm this finding and to evaluate the role of greater smoking rates among deployed personnel.

Zhu G, Tan M, Li Y, Xiang X, Hu H, Zhao S (2009) Accumulation and distribution of uranium in rats after implantation with depleted uranium fragments. J Radiat Res (Tokyo) 50:183-192.
Abstract: PURPOSE: The aim of our study was to clarify the accumulation and distribution of uranium in depleted uranium (DU) implanted rats. MATERIALS AND METHODS: Male Sprague-Dawley rats were surgically implanted in gastrocnemius muscle with DU fragments at 3 dose levels (low, medium and high), and biologically inert tantalum (Ta) fragments were used as controls. At 1 day and 7, 30, 90, 180 and 360 days after implantation, the rats were euthanized and tissue samples including serum and urine were collected to analyze the uranium levels by inductively coupled plasma-mass spectrometry (ICP-MS). RESULTS: At all time points, uranium levels in all the DU implanted groups were higher than that in Ta control group, and uranium concentrations in kidney and bone were significantly

greater than that in other tissues. Otherwise, uranium concentrations increased with a close correlation to the implanted DU doses and duration of exposure, with a peak at 90 days post-implantation, after which followed by a decreasing period, but still maintained at a relatively high level even at 360 days post- implantation. The uranium concentrations in bone were 6.92 +/- 0.97 µg U/g, 16.35 +/- 1.67 µg U/g and 21.64 +/- 3.68 µg U/g in the low-, medium- and high-dose group animals, while values in kidney tissues were 10.66 +/- 1.10 microg U/g, 14.06 +/- 1.28 µg U/g and 17.79 +/- 2.87 µg U/g, respectively, at 360 days post-implantation. CONCLUSION: It was concluded that kidney and bone are the primary reservoirs for uranium redistributed from intramuscularly embedded fragments, and the accumulations in kidney, bone and many other tissues suggest the potential for unanticipated physiological consequences of chronic exposure to DU.

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 2000-2009, and the number of research projects in which the Federal Government has invested.

The appropriated funds for FY 2000 through 2009, centrally obligated to each project, are shown in Appendix C and summarized in Table IV-1. Federal funding for GW research totaled approximately $267 million during this period. Funds obligated for these projects prior to FY 2000 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 2000 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 2000-2009) Funding Trends for GW Research in Millions of Dollars

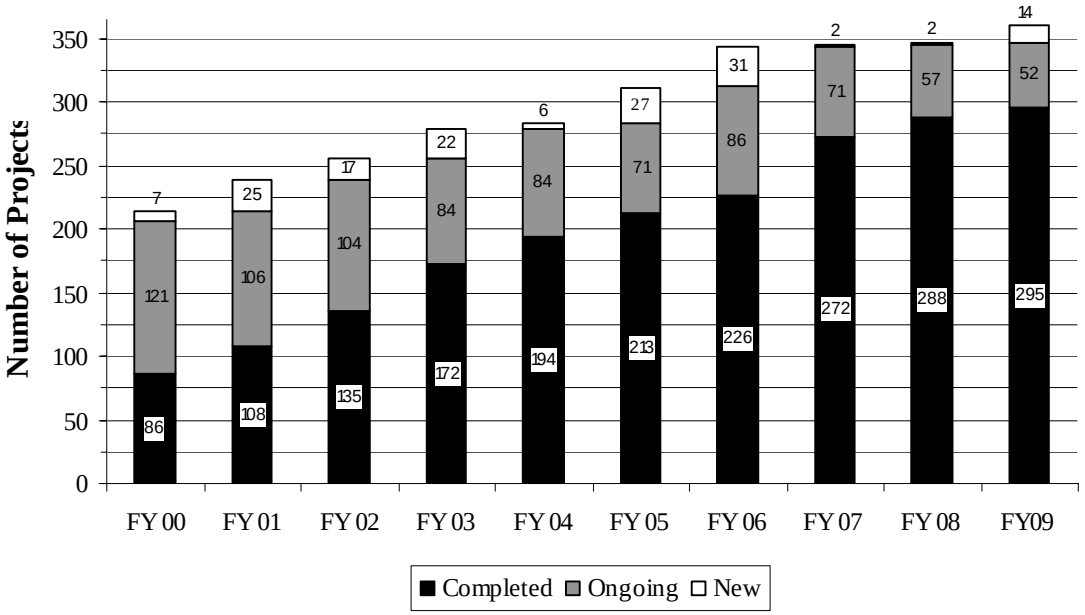
Department	FY '00	FY '01	FY '02	FY '03	FY '04	FY '05	FY '06	FY '07	FY '08	FY '09	Total Costs FY '00-'08
DoD	$ 23.8	$ 31.6	$ 18.8	$ 16.4	$ 11.1	$ 10.1	$ 10.1	$ 3.4	$ 11.7	$ 3.1	**$ 140.1**
HHS	$ 1.6	$ 1.0	$ 0.8	$ 1.0	$ 0.5	$ 0.5	$ 0.4	$ 0.4	$ 0.4	$ 0	**$ 6.6**
VA	$12.0	$ 8.6	$ 4.5	$ 5.7	$ 7.6	$ 9.5	$12.9	$ 22.0	$ 21.6	$ 15.7	**$ 120.1**
Total	**$ 37.4**	**$ 41.2**	**$ 24.1**	**$ 23.1**	**$ 19.2**	**$ 20.1**	**$ 23.4**	**$ 25.8**	**$ 33.7**	**$ 18.8**	**$ 266.8**

Funding for FY 2008 in the table above differs from the value reported in the Annual Report for 2008 due to the delayed start of 12 projects funded through the the FY08 appropriation for the Gulf War Illness Research (GWIRP) managed by the Congressionally Directed Medical Research Program (CDMRP) at DoD.

VA, DoD, and HHS sponsored a total of 361 distinct research projects on GWVI during the period of FY 1992 through FY 2009. 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.

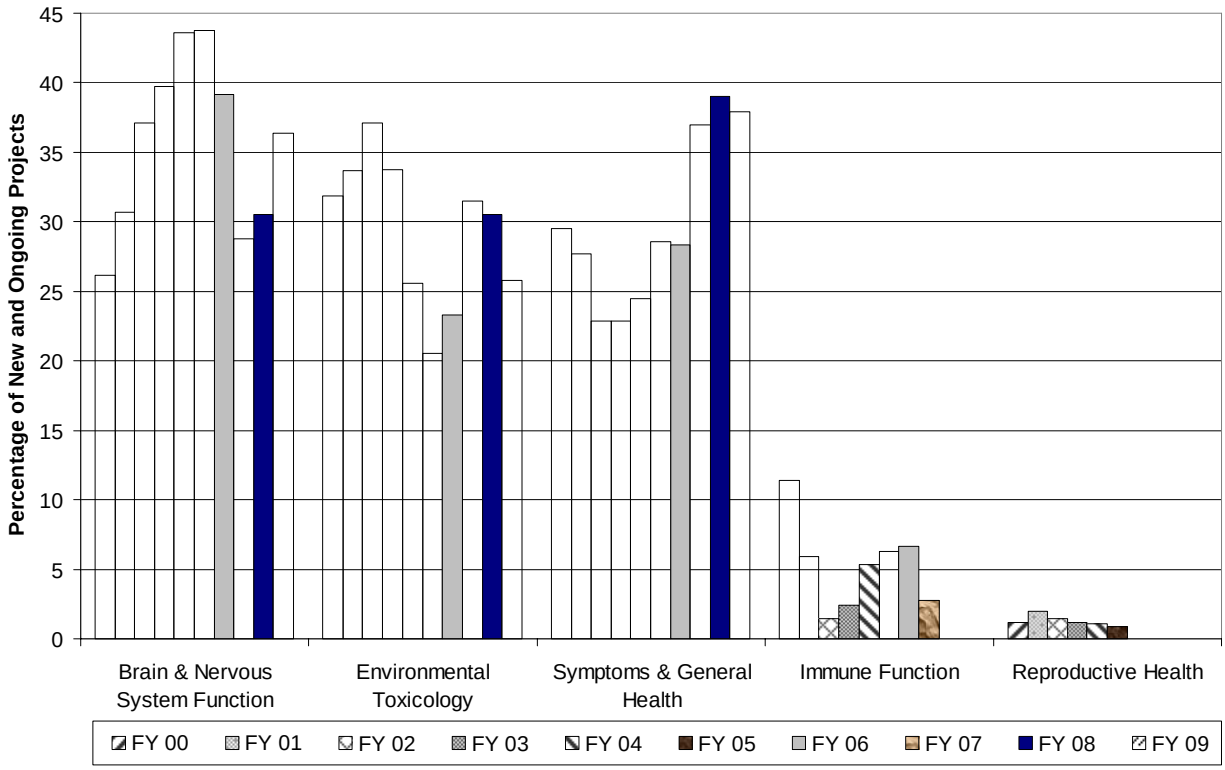
The numbers of new, ongoing and completed projects for FY 2000 - FY 2009 are shown in Figure IV-1. As of September 30, 2009, 295 projects (82 percent of the 361 projects) were completed, and 66 projects (18 percent) were new or ongoing; the numbers of new, ongoing, and completed projects for each fiscal year are shown in Figure IV-1.

Figure IV-1. Cumulative Number of Funded Projects (FY 2000 – FY2009)



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 2009 new and ongoing research assigned to Brain and Nervous System Function, Environmental Toxicology and General Health and Symptoms has represented 94.8 ± 1.4 percent of all 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 entered into a contractual agreement with the University of Texas Southwestern (UTSW) Medical Center for research related to illnesses affecting Veterans of the 1990-1991 Gulf War. However, because of contracting issues with UTSW, new task orders under this contract were not accepted for all of FY 2009 and the last two option years of the contract have not been exercised.

B. Portfolio Review

The Federal Gulf War research portfolio is increasingly focused on identifying potential new treatments (clinical trials, including complementary medicine approaches) for ill GW Veterans and identifying new diagnostic markers of disease and potential therapeutic targets to develop new therapies.

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)

Twelve projects were funded through the FY08 appropriation for the Gulf War Illness Research Program (GWIRP) managed by the Congressionally Directed Medical Research Program (CDMRP) at DoD, but did not start until FY 2009. These projects focused on Brain and Nervous System Function (3), Environmental Toxicology (2), and Symptoms and General Health (7).

*DoD-179, "Mechanisms of Mitochondrial Defects in Gulf War Syndrome" is designed to characterize mitochondrial function in 50 ill Gulf War Veterans using blood and skin cells tocharacterize precisely how mitochondria are working through detailed investigation of mitochondrial enzyme function, of mitochondria within living cells, of mitochondrial proteins, and of mitochondrial genes. Multiple lines of evidence suggest that the mitochondria are not functioning properly in GWVI and in CFS. Hence, detailed investigation of mitochondrial dysfunction in GWVI is a priority.

*DoD-180, "Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue" will study the proteins in the fluid around the brain as well as blood and other fluids to identify patterns of proteins and other mediators that begin to suggest a cause, or causes, for the fatigue and related symptoms in ill GW Veterans.

*DoD-181, "Effectiveness of Acupuncture in the Treatment of Gulf War Illness" is a clinical trial designed to evaluate acupuncture as an effective treatment for ill GW Veterans. Acupuncture has already been used successfully to reduce many of the key symptoms reported -- fatigue, irritability, anxiety, insomnia, and pain.

*DoD-182, "Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness" is a double-blinded clinical trial designed to test if naltrexone and dextromethorphan are effective in treating ill Gulf War veterans. Each participant will receive naltrexone for three months, dextromethorphan for three months and a placebo for three months, with a one-month period of no medication between each course of treatment.

*DoD-183, "Biomarkers of Gulf War Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation" is a follow-up to a VA-funded pilot study that found evidence of excessive blood clotting in veterans with Gulf War Veterans' Illnesses (GWVI). Blood from Gulf War Veterans with and without GWVI will be examined with an expanded panel of tests to identify additional evidence of excessive blood clotting in volunteers with GWVI. The goals are to develop effective ways to diagnose and to treat GWVI. The information generated by this study may lead directly to new clinical studies.

*DoD-184, “Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the Gulf War Veterans' Illnesses” use flupirtine, an approved drug that has been shown to improve cognition, learning and memory, and diminish muscular pain, in an animal model for Gulf War Veterans’ Illnesses (GWVI). The focus will be to investigate the protection and/or treatment of cognitive impairment and muscle weakness, the two hallmarks of GWVI.

*DoD-185, “Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model” will use an animal model to evaluate (1) molecular, cellular, and functional indices of neuroinflammation in mice exposed to GWVI-relevant agents and conditions; (2) the contribution of high physiological stress to neuroinflammation in this model; and (3) an FDA-approved atypical, nonsteroidal, anti-inflammatory agent as a potential therapeutic for GWVI symptoms related to neuroinflammation.

*DoD-186, “Small Intestinal Microbial Community in Gulf War Illness” will test three hypotheses (1) that small intestinal bacterial overgrowth is present in GWVI patients using quantitative PCR of total microbes on small intestinal mucosal biopsy tissue; (2) that the microbial diversity may be dominated by sulfate-reducing bacteria in GWVI patients and different from controls; and (3) that the quantity and diversity of microbes are reduced by antibiotic treatment.

*DoD-187, “The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies” utilizes an acute aerobic exercise paradigm and measurement of peripheral blood mononuclear cell (PBMC) gene expression by microarray along with immune and neuroendocrine marker assessments in 25 GWVI and 25 control subjects matched for age, gender, deployment to the Gulf War, and body mass index (BMI). The immune and genomic data will be collected at eight time points before and after an exercise stress challenge. By analyzing the flow of information through regulatory networks a foundation will be established for identifying complementary mechanisms that could be harnessed to restore normal network function.

*DoD-188, “Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness” will test the hypothesis that the respiratory symptoms in GWVI result from enhanced airway sensitivity to irritants and then address how changes in airway epithelial cells may promote self-perpetuating enhanced airway sensitivity.

*DoD-189, “Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers”will use a combination of two novel techniques to produce subunit-selective, water-soluble, and nanomolar affinity potentiators, that are selective to GluR2, a key AMPA receptor subunit involved in memory and a number of neurological disorders and diseases. Clinical studies have shown that AMPA receptor potentiators are cognitive enhancers and that the use of these potentiators is beneficial to memory and to the treatment of some cognitive disorders and diseases, such as depression and memory loss, which are two of the most common symptoms associated with GWVI.

*DoD-190, “Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness” will examine whether application of pyridostigmine bromide (PB) and the pesticides DEET and permethrin to mice will result in memory impairment of hippocampal origin and will allow modelling of the neurocognitive abnormalities of GWVI. The expectation is that mice with a genetic predisposition to develop memory problems will experience more severe cognitive impairment in response to exposure to these agents.

Department of Veterans Affairs (VA)

VA initiated funding for 2 new projects during FY 2009 focused on Brain and Nervous System Function (1) and Symptoms and General Health (1).

VA-153, “Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex” will test the hypothesis that symptoms of veterans with GWVI may depend on the abnormal bacterial gas production, associated with small intestinal bacterial overgrowth (SIBO) by comparing the prevalence of SIBO in ill Gulf War Veterans vs. healthy Veterans (controls). Changes in symptoms pre-& post-treatment will be correlated with a specific antibiotic with plasma & urine thiosulfate levels & bacterial fermentation products.

VA-154, “Imaging Pain Modulation in Gulf War Veterans with Chronic Muscle Pain” is a renewal of VA-096 will address 3 specific aims; (1) determine the influence of pain anticipation on fMRI responses to non-painful stimuli in

GW Veterans with chronic musculoskeletal pain (CMP) compared with healthy and rheumatoid arthritis (RA) controls; (2) determine the influence of attention to pain on central processing of painful stimuli in GW Veterans with CMP compared with healthy and RA controls; and (3) determine whether white matter tract structure in the brain is altered in GW veterans with CMP compared with healthy and RA controls.

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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
DoD-179	Mechanisms of Mitochondrial Defects in Gulf War Syndrome
DoD-180	Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue
DoD-181	Effectiveness of Acupuncture in the Treatment of Gulf War Illness
DoD-182	Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness
DoD-183	Biomarkers of Gulf War Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation
DoD-184	Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the Gulf War Veterans' Illnesses
DoD-185	Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model
DoD-186	Small Intestinal Microbial Community in Gulf War Illness
DoD-187	The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies
DoD-188	Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness
DoD-189	Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers
DoD-190	Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness

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 with UTSW
VA-151	Genetic Epidemiology of ALS
VA-152	Multiple Sclerosis in Gulf War Veterans
VA-153	Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex
VA-154	Imaging Pain Modulation in Gulf War Veterans with Chronic Muscle Pain

Appendix B

Project List by Research Focus Areas

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
	Diagnosis	DoD-165	Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military - BALSAM
	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;	Symptoms Chemical Weapons	DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity
Immune Function; Symptoms and General Health	Symptoms	VA-005 B	Physiological and Psychological Assessments of Persian Gulf Veterans
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
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

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
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
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

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
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
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; Environmental Toxicology	Symptoms;	VA-008	Psychological Test Data of Gulf War Veterans Over Time

Brain and Nervous System Function

Development

Research Focus	Project Focus	Project	Project Title
	Diagnosis	HHS-013	ALS Biomarkers in the Cerebrospinal Fluid
	Treatment	DoD-189	Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers
Environmental Toxicology	Treatment; Exposure; Symptoms	DoD-184	Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the Gulf War Veterans' Illnesses
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

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
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	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	VA-150	Gulf War Veterans Illnesses' Research IDIQ Contract

Brain and Nervous System Function

Epidemiology

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Diagnosis	VA-151	Genetic Epidemiology of ALS Veterans
Symptoms and General Health	Symptoms	VA-152	Multiple Sclerosis in Gulf War Veterans
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 (See also VA-088)
Symptoms and General Health	Diagnosis; Symptoms;	HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18
Symptoms and General Health	Diagnosis; Symptoms;	VA-088	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also DoD-154)

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
	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 Reasonance 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	Exposure; Symptoms;	DoD-190	Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness
Environmental Toxicology;	Treatment; Exposure; Immune Function	DoD-185	Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model

Brain and Nervous System Function

Mechanistic

Research Focus	Project Focus	Project	Project Title
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 Illness
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
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; Symptoms;	VA-102	Cholinergic and Monoaminergic Influences on Sleep

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
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	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
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide Symptoms
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

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

Environmental Toxicology

Development

Research Focus	Project Focus	Project	Project Title
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
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

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

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
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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
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 Modeling
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
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	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	Exposure	DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
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
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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
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
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

Immune Function and Infectious Diseases

Clinical

Research Focus	Project Focus	Project	Project Title
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)

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

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?

Immune Function and Infectious Diseases

Mechanistic

Research Focus	Project Focus	Project	Project Title
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

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

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

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	DoD-181	Effectiveness of Acupuncture in the Treatment of Gulf War Illness
	Treatment; Symptoms	DoD-186	Small Intestinal Microbial Community in Gulf War Illness
	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
	Treatment; Symptoms;	VA-153	Bacterial Overgrowth Associated with Chronic Multi- Symptom Illness Complex
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

Symptoms and General Health

Clinical

Research Focus	Project Focus	Project	Project Title
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
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	Symptoms	VA-154	Imaging Pain Modulation in Gulf War Veterans with Chronic Muscle Pain
Brain and Nervous System Function	Symptoms; Diagnosis;	DoD-180	Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of 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;	DoD-182	Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' 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 (13)
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
Immune Function	Symptoms	DoD-187	The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies
Immune Function	Symptoms	DoD-188	Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War 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
Immune Function	Symptoms; Diagnosis;	DoD-183	Biomarkers of Gulf War Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation

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 and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-150	Validation Study of Gulf War Deployment Files
	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; Exposure;	DoD-073	Post-deployment Morbid Stress, Behavior and Health: 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
	Symptoms	VA-001	Mortality Follow-up Study of Persian Gulf 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
Brain and Nervous System Function	Symptoms	DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans
Brain and Nervous System Function	Symptoms	DoD-142	Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
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	Millenium 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)
		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

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-179	Mechanisms of Mitochondrial Defects in Gulf War Syndrome
	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
Environmental Toxicology	Exposure; Symptoms	DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness

Symptoms and General Health

Mechanistic

Research Focus	Project Focus	Project	Project Title
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, 2009)

NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH FROM FY 2000-2009

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 1992-2009 are listed, only the financial data for FY 2000-2009 (a 10-year window) are shown in Appendix C; Totals for FY '00-'08 do not include funds obligated in FY 1992-1999. Projects that received all of their obligated funds prior to FY 2000 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 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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	$0										$0
DoD-008	Program DoD-8.	C											$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	$0	$0	$0	$0							$0
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	$306,000	$195,000	$225,000							$1,021,000
DoD-019	Persian Gulf Veterans Health Tracking System	C	$0	$0	$100,000	$50,000							$150,000

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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
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
DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome	C	$0										$0
DoD-032	Neuropsychological Functioning in Persian Gulf Era Veterans	C											$0
DoD-033	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity	C											$0
DoD-034	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents	C											$0
DoD-035	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.	C	$0	$0									$0
DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms	C											$0
DoD-037	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats	C											$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	$124,868	$0									$124,868
DoD-040	Psychological and Neurobiological Consequences of the Gulf War Experience	C	$0	$0									$0
DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans	C	$0										$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment	C	$0	$0									$0
DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions	C											$0
DoD-045	Air Force Women's Health Surveillance Study	C	$0	$99,628	$0								$99,628
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
DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways	C											$0
DoD-051	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses	C	$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	$217,137	$0									$217,137
DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure	C	$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

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine	C	$0	$0									$0
DoD-057	Physiologic Effects of Stress in Gulf War Veterans	C	$0	$0	$0								$0
DoD-058	Illness Among Persian Gulf War Veterans: Case Validation Studies	C	$4,264	$267,337	$0	$0	$0						$271,601
DoD-059	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis	C	$0	$0									$0
DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness	C											$0
DoD-061	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid	C	$0										$0
DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice	C											$0
DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity	C	$0										$0
DoD-064	Individual Differences in Neurobehavioral Effects of Pyridostigmine	C	$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
DoD-066	Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction	C	$140,319	$0									$140,319
DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria	C											$0
DoD-069	Five Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents	C	$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	$0	$0									$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
DoD-071	A Comparison of Post Deployment Hospitalization Between Vietnam and Gulf War Veterans	C	$0										$0
DoD-072	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals	C	$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
DoD-074	Relationship of Stress Exposures to Health in Gulf War Veterans	C	$0	$0	$0								$0
DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides	C	$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
DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War	C	$0	$0	$0								$0
DoD-078	Experimental Models of Gulf War Syndrome	C	$0	$0	$0								$0
DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier	C	$0										$0
DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells	C	$0	$0	$0								$0
DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress	C	$0	$0	$0								$0
DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs	C	$0	$0	$0								$0
DoD-083	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism	C	$0	$0	$0								$0
DoD-084	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD	C	$0	$0	$0								$0
DoD-085	CNS Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms	C	$0	$0	$0								$0
DoD-086	Effects of Combat Stress on Structure and Function of the Hippocampus	C	$0	$0	$0	$0							$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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	$68,044	$0	$0							$68,044
DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD	C	$0	$0	$0								$0
DoD-089	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder	C	$0	$0	$0								$0
DoD-090	SPECT Benzodiazepine Receptor and MR Imaging in PTSD	C	$0	$0	$0								$0
DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors	C	$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
DoD-093	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up	C	$0	$0									$0
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	$206,727	$0	$0								$206,727
DoD-095	Development of Diagnostic tools and alternative treatment drugs for Leishmania	C	$1,500,000	$1,500,000	$1,500,000								$4,500,000
DoD-096	Deployment Health Center	C	$1,500,000	$2,250,000	$1,750,000	$1,750,000	$1,750,000	$0					$9,000,000
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	$146,742	$151,202	$151,000								$448,944
DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans	O	$188,000	$364,182	$0	$0	$0	$0	$0	$0	$0	$0	$552,182

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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	$204,205	$224,265	$0	$0							$428,470
DoD-100	Antibodies to Squalene	O	$0	$50,000	$487,333	$0	$0	$0	$0	$0	$0	$0	$537,333
DoD-101	Mechanisms in Chronic Multisymptom Illnesses	O	$5,542,189	$0	$4,786,192	$644,870	$4,781,952	$2,429,999	$0	$0	$0	$0	$18,185,202
DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans	C	$0	$253,793	$0	$281,950							$535,743
DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals	O	$46,315	$0	$0	$349,994	$242,424	$160,000	$326,570	$166,570	$0	$0	$1,291,873
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome	C	$9,311	$0	$0	$40,844							$50,155
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala	C	$0	$0	$0	$0	$0						$0
DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness	C	$0	$0	$0								$0
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity	C	$10,825	$0	$0	$0	$0						$10,825
DoD-108	Health Status of Current National Guard Members	C	$0	$264,375	$174,651	$0	$0	$0					$439,026
DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms	C	$147,523	$397,243	$0	$0							$544,766
DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy	C	$63,705	$0	$0								$63,705
DoD-111	Autonomic Dysfunction in Gulf War Veterans	C	$0	$0	$0	$189,609	$0	$0					$189,609
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	C	$0	$0	$0								$0
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects	C	$0	$0	$0	$0	$0						$0
DoD-114	A Re-examination of Neuropsychological Functioning in Persian Gulf War Veterans	C	$0	$0	$0								$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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	$2,000,000	$0	$0								$2,000,000
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							$1,000,000
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	$1,000,000	$0	$0								$1,000,000
DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents	C	$316,000	$0	$0								$316,000
DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development	C	$15,000	$15,000									$30,000
DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys	C	$30,000	$35,000									$65,000
DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys	C	$20,000	$15,000									$35,000
DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin	C	$0	$0	$0	$0	$0	$0					$0
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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DoD-126	Blood-Brain Barrier Transport of Uranium	O	$790,884	$0	$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	$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	$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	$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	$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	$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	$0	$434,795

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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	$3,145,000	$24,529,000
DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces	O	$295,000	$250,000	$300,000		$0	$0	$0	$0	$0	$0	$845,000
DoD-145	Early Intervention Research Program to Enhance Soldier Resilience	O		$250,000	$275,000	$275,000	$0	$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	$260,000	$412,000	$696,111	$292,530	$0	$0	$0				$1,660,641
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	$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 Assestment 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	$0	$1,639,601

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide	C				$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	$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	$0	$1,152,744
DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function	C				$1,041,751	$0	$0	$0	$0	$0		$1,041,751
DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin	C				$1,828,876	$0	$0	$0	$0	$0		$1,828,876
DoD-164	Efficacy of Adjunct Sleep Interventions For PTSD (EASI-PTSD)	C						$999,623	$0	$0	$0		$999,623
DoD-165	Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military - BALSAM	C						$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	C						$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	$0	$637,848
DoD-168	Developing Biomarkers for Fibromyalgia	O							$936,067	$0	$0	$0	$936,067
DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain	O							$840,574	$0	$0	$0	$840,574

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I	O							$208,353	$0	$0	$0	$208,353
DoD-171	Q10 for Gulf War Veterans	O							$718,261	$0	$0	$0	$718,261
DoD-172	CNDP1 Polymorphisms and Carnosine Therapy in GWI	O							$831,200	$0	$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	$0	$650,279
DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness	O							$687,530	$0	$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	$0	$767,061
DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome	C							$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	$0	$445,865
DoD-178	Analysis of Paraoxonase Status among US Navy Gulf War Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions	C							$73,153	$0	$0		$73,153
DoD-179	Mechanisms of Mitochondrial Defects in Gulf War Syndrome	O						$0	$0	$0	$440,674	$0	$440,674
DoD-180	Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue	O						$0	$0	$0	$921,000	$0	$921,000
DoD-181	Effectiveness of Acupuncture in the Treatment of Gulf War Illness	O						$0	$0	$0	$1,015,733	$0	$1,015,733
DoD-182	Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness	O						$0	$0	$0	$1,063,641	$0	$1,063,641
DoD-183	Biomarkers of Gulf War Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation	O						$0	$0	$0	$653,460	$0	$653,460
DoD-184	Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the Gulf War Veterans' Illnesses	O						$0	$0	$0	$311,135	$0	$311,135

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
DoD-185	Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model	O						$0	$0	$0	$718,326	$0	$718,326
DoD-186	Small Intestinal Microbial Community in Gulf War Illness	O						$0	$0	$0	$634,142	$0	$634,142
DoD-187	The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies	O						$0	$0	$0	$715,456	$0	$715,456
DoD-188	Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness	O						$0	$0	$0	$842,400	$0	$842,400
DoD-189	Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers	O						$0	$0	$0	$303,000	$0	$303,000
DoD-190	Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness	O						$0	$0	$0	$894,000	$0	$894,000
			$23,847,679	$31,587,006	$18,827,819	$16,419,497	$11,096,063	$10,091,848	$10,128,261	$3,417,570	$11,672,967	$3,145,000	$140,233,710

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Department of Health and Human Services Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
HHS-001	Health Assessment of Persian Gulf War Veterans from Iowa	C	$0	$0									$0
HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18	C	$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	$660,000	$0	$0								$660,000
HHS-006	Defining Gulf War Illness	C	$719,792	$200,000	$0								$919,792
HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid	C	$187,647	$0									$187,647
HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures	C	$0	$0									$0
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	$0	$2,263,635
			$1,567,439	$998,870	$799,814	$964,105	$466,126	$466,481	$455,587	$441,974	$433,467	$0	$6,593,863

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
VA-001	Mortality Follow-up Study of Persian Gulf Veterans	C	$176,440	$171,154	$128,496	$0							$476,090
VA-002	National Health Survey of Persian Gulf Veterans	C	$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
VA-002 C	VA National Survey of Persian Gulf Veterans - Phase III	C	$3,400,000	$2,344,427	$30,000								$5,774,427
VA-003	Use of Roster of Veterans Who Served in Persian Gulf Area	C											$0
VA-004	Boston Environmental Hazards Research Center Program	C	$229,500										$229,500
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	$326,900										$326,900
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
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

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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	$233,290										$233,290
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
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
VA-011	Neuropsychological Functioning in Veterans	C											$0
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	$41,540	$114,336	$119,600	$59,800							$335,276
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

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Department of Veterans Affairs Gulf War Research Funding

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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
VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder	C	$0										$0
VA-047	Retrospective Verification of Mustard Gas Exposure	C	$139,960										$139,960
VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance	C	$92,840	$45,000									$137,840
VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction	C	$141,696	$144,024	$125,862								$411,582
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
VA-053	Spouses and Children Program	C	$33,655	$12,934	$25,000								$71,589
VA-054	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress	C	$90,131	$86,895	$86,350	$72,700	$39,375						$375,451
VA-055	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)	C	$1,466,375	$1,981,963	$254,000								$3,702,338
VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)	C	$161,175										$161,175
VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)	C	$174,750										$174,750
VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)	C	$262,496										$262,496
VA-059	Demonstration Treatment Program for Gulf War Veterans With Unexplained Physical Symptoms (13)	C	$259,500										$259,500

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Department of Veterans Affairs Gulf War Research Funding

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VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans	C	$246,375										$246,375
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	$3,756,826	$1,971,233	$44,250								$5,772,309
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			$2,000,000
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
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

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VA-065 C	The importance of hydrogen peroxide detoxification in cellular protection	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
VA-067	Olfactory Functioning in Gulf War Veterans	C	$7,500	$7,500									$15,000
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	$6,204	$4,884	$4,900								$15,988
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	Millenium Cohort Study	O											$0
VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress	C				$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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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	O				$250,000	$281,000	$281,000	$449,990	$449,990			$1,711,980
VA-090A	Neuronal Hyperexcitability and Motor Neuron Regeneration	O											$0
VA-090B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders	O											$0
VA-090C	Developmental Differences in Alcohol Withdrawal Sensitivity	O											$0
VA-090D	Seizures and Neuroplasticity:Physiology and Biochemistry	O											$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
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

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VA-096	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain	C					$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	$274,432	$1,114,809
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	$93,226	$787,362
VA-108	Telemedicine Treatment for Veterans with Gulf War Illness	C						$185,714	$238,616	$224,916	$11,100		$660,346
VA-109	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics	O						$158,372	$306,912	$317,503	$321,148	$241,520	$1,345,455
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	C						$166,352	$110,152	$110,152	$110,152	$0	$496,808

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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	C						$42,206	$151,740	$115,772	$66,597	$0	$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
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	$560,455	$2,760,404
VA-126	Structural Magnetic Reasonance 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	$273,861	$934,483
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	$56,200	$345,630

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
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	$0	$25,880	$34,760
VA-135	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue	O							$6,744	$0	$0	$79,242	$85,986
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	$0	$603,587
VA-138	Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP	O							$226,773	$235,240	$258,136	$9,819	$729,968
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	$5,664,976	$8,739,543
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	$112,400	$691,260
VA-146	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route	O							$161,687	$256,159	$245,295	$195,214	$858,355
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	$273,801	$672,563
VA-150	Gulf War Veterans Illnesses' Research IDIQ Contract with UTSW	O								$15,000,000	$15,000,000	$6,972,481	$36,972,481

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	TOTALS FY 00-09
VA-151	Genetic Epidemiology of ALS Veterans	O									$2,116,602	$377,557	$2,494,159
VA-152	Multiple Sclerosis in Gulf War Veterans	O									$122,010	$137,791	$259,801
VA-153	Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex	O										$8,377	$8,377
VA-154	Imaging Pain Modulation in Gulf War Veterans with Chronic Muscle Pain (renewal of VA-096)	O										$300,782	
			$12,020,519	$8,576,675	$4,512,676	$5,746,467	$7,644,559	$9,484,679	$12,942,066	$21,820,885	$21,636,369	$15,658,014	$120,042,909

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