

FISCAL YEAR 2011 APPROPRIATIONS REQUESTS Department of Defense

Multisymptom illnesses have been reported among military personnel returning from combat since the Civil War¹. However, following Operations Desert Shield and Desert Storm in the Persian Gulf (1990-1991), the scope and impact of such illnesses received heightened attention and have been studied by the Department of Veterans Affairs, the National Institutes of Health, the Centers for Disease Control & Prevention, and the Institute of Medicine. A seminal study comparing the health of deployed and non-deployed Gulf War era veterans established a case definition for chronic multisystem illness, characterized by fatigue, cognition-mood and musculoskeletal symptoms, and also highlighted the overlap of veterans' illnesses with chronic fatigue syndrome (CFS)². A report issued in 2008 by the Research Advisory Committee on Gulf War Veterans' Illnesses states that at least one-fourth of the 697,000 veterans of the Gulf War have experienced multisystem illnesses of this nature³.

Service men and women returning from Operation Enduring Freedom and Operation Iraqi Freedom are also experiencing chronic multisystem illnesses. Female service members' expanded involvement in these conflicts may present new post-deployment health issues as they return from Iraq and Afghanistan⁴. CFS occurs at higher rates among women compared to men and the prevalence of CFS among veterans of the current military actions may be even higher than seen following the Persian Gulf War.

To better understand the prevalence and impact of CFS among active duty military and veterans and how to effectively intervene and prevent it, CFS should be made an eligible research topic in the Peer-Reviewed Medical Research Program (PRMRP) targeted for biomedical research funding through the U.S. Department of Defense in fiscal year 2011.

THE BURDEN OF ILLNESS IMPOSED BY CFS

CFS is defined as severe, incapacitating fatigue of at least six months duration that is not improved by bed rest and that may be worsened by physical or mental activity. This disabling fatigue is accompanied by: unrestorative sleep, problems with concentration and short-term memory, joint and muscle pain, tender lymph nodes, sore throat and headache. A hallmark of

¹ Hyams KC, Wignall FS, Roswell R. 1996. War syndromes and their evaluation: From the U.S. Civil War to the Persian Gulf War. *Annals of Internal Medicine* 125(5):398-405.

² Fukuda K, Nisenbaum R, Stewart G, et al. Chronic multisymptom illness affecting air force veterans of the gulf war. *JAMA*. 1998;280:11.

³ Research Advisory Committee on Gulf War Veterans' Illnesses. Gulf War illness and the health of Gulf War veterans. U.S. Government Printing Office. Nov. 2008.

http://sph.bu.edu/insider/images/stories/resources/annual_reports/GWI%20and%20Health%20of%20GW%20Veterans_RAC_GWVI%20Report_2008.pdf. Accessed Feb. 1, 2010.

⁴ Street A, Vogt D, Dutra L. A new generation of women veterans: stressors faced by women deployed to Iraq and Afghanistan. *Clin Psychol Rev*. 2009. Dec; 29(8):685-94.

the illness is postexertional malaise, a worsening of symptoms following even very modest physical or mental exertion that can persist for days or weeks.⁵ As stated above, CFS bears striking similarity to multisymptom illnesses described in veterans, particularly those returning from the Persian Gulf conflicts of 1990-1991 and 2002 to the present. The effects of CFS on the patient are very similar to those experienced by individuals suffering traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD), both occurring at high rates among veterans of Operations Iraqi Freedom and Enduring Freedom.

The burden of illness and disability in the civilian population caused by CFS is profound:

- CFS affects more than one million people in the U.S.⁶ yet only 20% have been diagnosed or receive appropriate medical care.
- The physical symptoms that are characteristic of CFS are common and account for more than half of all outpatient visits in the U.S.⁷
- Population-based studies of CFS have found at least 25% of people with CFS are receiving disability or unemployed⁸. CFS can be as disabling as chronic obstructive pulmonary disease, end-stage renal failure and multiple sclerosis.
- Economic impact studies have determined that costs to the U.S. economy due to lost productivity and medical costs associated with CFS exceed \$24 billion each year^{9,10}.

According to a recent search for CFS diagnoses in the Defense Medical Surveillance System (DMSS), more than 5,000 military personnel, ages 17-39 have been diagnosed with CFS between 1999-2009¹¹. This is likely to be a vast underestimate, given the frequent use of other diagnostic codes for CFS symptoms, and underrecognition of CFS by military health care professionals that mirrors the low rate of diagnosis (20 percent) in the civilian population. The Veterans Affairs medical system strives to deliver care to patients suffering service-related injury or illness through the War Related Injury and Illness Study Centers¹².

THE CASE FOR INCLUDING CFS AS AN ELIGIBLE PRMRP RESEARCH TOPIC

There are approximately 5,000 studies in the peer-reviewed literature about CFS, but few have studied military personnel or been applied to military settings for health care delivery. The physical and cognitive symptoms of CFS by definition make it challenging to sustain military readiness for those who suffer from this condition.

⁵ Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Ann Intern Med.* 1994 Dec 15;121(12):953-9.

⁶ Reeves WC, Jones JF, Maloney E, et al. Prevalence of chronic fatigue syndrome in metropolitan, urban, and rural Georgia. *Population Health Metrics.* 2007;5:5.

⁷ Jackson JL, Kroenke K. Prevalence, impact, and prognosis of multisomatoform disorder in primary care: a 5-year follow-up study. *Psychosom Med.* 2008 May;70(4):430-4. Epub 2008 Apr 23.

⁸ Solomon L, Reeves WC. Factors influencing the diagnosis of chronic fatigue syndrome. *Arch Intern Med.* 2004 Nov 8;164(20):2241-5.

⁹ Reynolds KJ, Vernon SD, Bouchery E, Reeves WC. The economic impact of chronic fatigue syndrome. *Cost Eff Resour Alloc.* 2004 Jun 21;2(1):4.

¹⁰ Jason LA, Benton MC, Valentine L, Johnson A, Torres-Harding S. The Economic impact of ME/CFS: Individual and societal costs. *Dyn Med.* 2008 Apr 8;7:6.

¹¹ Personal communication with Renata Engler, M.D., Walter Reed Army Medical Center. September 2009.

¹² Wallin MT, Chapman JC. Evaluation of combat veterans. *Forum.* Dept. of Veterans Affairs Research and Development Service. Sept. 2005. <http://www.academyhealth.org/files/publications/forum/sep05.pdf>, accessed Feb. 1, 2010.

Studies of CFS have documented abnormalities in the immune, endocrine, autonomic nervous and central nervous systems. CFS has also been linked to various environmental exposures, including viruses, neurotoxins and chronic stress. These linkages echo many of the exposures faced by military service personnel in conflict areas – living in extreme climates and environments, extreme physical exertion, multiple vaccinations, exposure to foreign viruses and microbes, toxic chemicals and neurotoxins. These factors may put service men and women at a higher risk of developing CFS. A recent study that detected a new human retrovirus, XMRV, in CFS cases¹³, provides possible causal and pathophysiology clues for CFS and would be important to examine in military personnel and family members who report CFS or CFS-like symptoms.

The Peer Reviewed Medical Research Program (PRMRP) at the US Department of Defense provides support for research with clear scientific merit with direct relevance to the health of the warfighter, the military family and the American public. PRMRP Congressional appropriations totaled \$50 million in FY09 and have provided funding for 247 projects in more than 60 topic areas. Many projects funded by the PRMRP have begun to yield military combat health support technologies and products in the areas of Combat Casualty Care, Military Infectious Diseases, Military Operational Medicine, Chronic Disease Management, and Medical Chemical and Biological Defense, thus complementing the current USAMRMC Core priorities. CFS is an area of immediate and ripe opportunity for contributing to the improved health and readiness of our troops and their family members.

Given the significant health, safety and economic impacts of disabling chronic fatigue and chronic fatigue syndrome (specifically) on military servicemen and women, and the unique risks that military servicemen and women are exposed to, **we request that the Appropriations Subcommittee on Defense make CFS an eligible research topic in the Peer-Reviewed Medical Research Program (PRMRP) targeted for biomedical research funding through the U.S. Department of Defense in Fiscal Year 2011.**

INFORMATION ABOUT XMRV AND CFS

In the Oct. 8, 2009 issue of *Science*, researchers at the Whittemore Peterson Institute, the Cleveland Clinic and the National Cancer Institute reported that 67 percent of 101 CFS patients tested positive for infection with xenotropic murine leukemia-related retrovirus (XMRV), a gammaretrovirus associated with a subset of prostate cancer. 3.7 percent of 218 healthy subjects tested were positive for the virus. Further research is under way at several other institutions in the U.S. and other countries and more reports are forthcoming. There is currently no FDA-approved test available for XMRV and clinical studies of antiviral and antiretroviral treatments must be conducted to test their efficacy against XMRV infection and their safety in XMRV-positive patients. The Department of Health and Human Services is presently coordinating a study to assess whether XMRV poses a risk to the safety of the blood supply, based on the identification of XMRV in 3.7 percent of the healthy subjects tested.

*For more information about CFS please contact the **CFIDS Association of America** www.cfids.org, info@cfids.org, or 704-365-2343*

¹³ Lombardi VC, Ruscetti FW, Gupta JD, et al. Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome. *Science*. 2009;1179052.