

FISCAL YEAR 2011 APPROPRIATIONS REQUESTS Labor, Health and Human Services, Education and Related Agencies

In order to advance research toward objective diagnosis, effective treatment and prevention of chronic fatigue syndrome (CFS), the CFIDS Association of America requests that the FY11 Labor, Health and Human Services Appropriations bill include the following proposed report language:

National Institutes of Health: Important advances have been made in identifying markers for the diagnosis and treatment of CFS. The detection of a human retrovirus, XMRV, in people with CFS, as well as healthy people, indicates a possible risk to the nation's blood supply that is being investigated by the Department of Health and Human Services. This development warrants enhanced priority and funding for the millions of Americans affected by CFS. To maximize public and private research investments in studies that can accelerate progress, the Committee urges the Director to support increased intramural staffing for CFS and increased funding for a multidisciplinary CFS research network to develop standards, share and consolidate data, support adequately powered genetic, genomic and intervention studies, and enhance collaboration across the agency.

Centers for Disease Control and Prevention: The Committee urges the CDC to follow recommendations made by the DHHS CFS Advisory Committee and the 2008 peer review panel to prioritize laboratory efforts aimed at the identification of diagnostic subtypes and therapeutic biomarkers with increasing efforts in viral etiology. Intervention, including vaccination studies, against pathogens with known associations with CFS should be pursued in collaboration between intramural CDC expertise and other agencies and investigators to support adequately powered genetic, genomic and intervention studies. The Committee further supports openness in publicly supported research and encourages the CDC to share data accumulated since 1984 by the CDC CFS research program with CFS research stakeholders.

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 the illness is postexertional malaise, a worsening of symptoms following even very modest physical or mental exertion that can persist for days or weeks.¹

¹ 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.

The burden of illness and disability caused by CFS is profound:

- CDC estimates that CFS affects more than one million people in the U.S.² 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.³
- Population-based studies of CFS have found at least 25% of people with CFS are receiving disability or unemployed⁴. 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^{5,6}.

THE CASE FOR A CFS RESEARCH NETWORK

In spite of 25 years of research and more than 5,000 studies in the peer-reviewed literature, there is still no known cause, diagnostic test or universally effective treatment for CFS.

Abnormalities in the immune, endocrine, autonomic nervous and central nervous systems have been documented in the scientific literature. Unfortunately, cross-sectional case-control studies have provided subtle clues, but no consensus, about objective diagnosis and effective treatment of CFS^{7,8,9}. Much of the uncertainty over the appropriate management of CFS stems from a lack of consistency between research studies due to these five factors:

1. Significant heterogeneity in the patient groups both within and between research centers^{10,11};
2. Lack of standardized study protocols and laboratory methodology;
3. Reliance solely upon cross-sectional study designs involving convenience samples;
4. Inappropriate selection of comparison subjects; and,
5. Variation in biologic sample type, collection and processing.

² 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.

³ 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.

⁴ Solomon L, Reeves WC. Factors influencing the diagnosis of chronic fatigue syndrome. *Arch Intern Med*. 2004 Nov 8;164(20):2241-5.

⁵ 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.

⁶ 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.

⁷ Whiting P, Bagnall AM, Sowden AJ, et al. Interventions for the treatment and management of chronic fatigue syndrome: a systematic review. *JAMA* 2001; 286: 1360-1368.

⁸ Royal Australasian College of Physicians Working Group. Chronic fatigue syndrome - Clinical practice guidelines 2002. *Med J Aust* 2002; 176: S17-55.

⁹ Afari N, Buchwald D. Chronic fatigue syndrome: a review. *Am J Psychiatry* 2003; 160:221-236.

¹⁰ Vollmer-Conna U, Aslakson E, White PD. An empirical delineation of the heterogeneity of chronic unexplained fatigue in women. *Pharmacogenomics*. 2006 Apr;7(3):355-64.

¹¹ Wilson A, Hickie I, Hadzi-Pavlovic D, et al. What is chronic fatigue syndrome? Heterogeneity within an international multicentre study. *Aust & NZ J Psych* 2001; 35: 520-27.

The creation of a coordinated, collaborative CFS research network will:

- Build, support and link a critical mass of innovative and credible researchers focused on early detection, objective diagnosis and effective treatment and to create, identify and leverage new private and federal funding sources and opportunities for CFS investigators.
- Allow investigators to assess one another's work, optimize aspects of study designs and identify possible synergies among investigators and studies.
- Actively foster, facilitate and participate in innovative and collaborative applications to funding opportunity announcements (FOAs) issued by federal agencies like the NIH's program announcement on CFS¹².
- Augment NIH-supported investigators in partnership with NIH as well as NIH-supported initiatives.
- Establish "best practices" and "standard operating procedures" and develop access to well-characterized patient samples and support adequately powered genetic, genomic and intervention studies.

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.¹³ Only 3.7 percent of 218 healthy subjects tested were positive for the virus. At the end of the article, the authors raise questions about this discovery, including "Is XMRV infection a causal factor in the pathogenesis of CFS or a passenger virus in the immunosuppressed CFS patient population?" Additional questions were raised after a Jan. 6, 2010 report in the online journal *PLoS ONE* by researchers at the Imperial College in London who found no evidence of XMRV by polymerase chain reaction testing in 186 CFS patients' banked samples¹⁴. Laboratory methods and patient selection criteria differed between the two studies in substantial ways. 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,
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¹² <http://grants.nih.gov/grants/guide/pa-files-archive/PA-08-246.html>, accessed Jan. 29, 2010.

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.

¹⁴ Erlwein O, Kaye S, McClure MO, et al. Failure to Detect the Novel Retrovirus XMRV in Chronic Fatigue Syndrome. *PLoS ONE*. 2010;5(1):e8519.