

Gulf War Vets May Face Increased ALS Risk

BY MARY ELLEN SCHNEIDER
New York Bureau

Veterans of the 1990-1991 Persian Gulf War may be at increased risk for developing psychological conditions and their service may be associated with a greater chance of developing amyotrophic lateral sclerosis, according to a report by the Institute of Medicine.

The link between military service in the Gulf and developing amyotrophic lateral sclerosis (ALS) is still inconclusive, but the committee that prepared the Institute of Medicine (IOM) report called for follow-up studies to evaluate the prevalence of the condition among Gulf War veterans.

The report, which was released in September, is based on a review of 850 studies including both self-reported data from veterans and studies using objective measures of symptoms and exposures. The report was sponsored by the Department of Veterans Affairs.

The IOM committee did not find evidence to declare a definitive link between reports of multisymptom illness and Gulf War service. Although nearly 30% of Gulf War veterans reported that they experienced some type of multisymptom illness, compared with about 16% among nondeployed veterans, there were no objective test results to support those reports, the IOM committee wrote. The multisymptom conditions that were reported more commonly among Gulf War veterans include fibromyalgia, chronic fatigue syndrome, and multiple chemical sensitivity.

The report also notes that there is no single unique cluster of symptoms that make up Gulf War illness.

"Gulf War veterans consistently report experiencing a wide range of symptoms, and this is the case for both American veterans and military personnel from Canada, Australia, and other countries who served in the Persian Gulf," Dr. Lynn R. Goldman, IOM committee chair and professor of occupational and environmental health at Johns Hopkins University in Baltimore, said in a statement.

The Institute of Medicine report also found that deployment to the Gulf puts veterans at an increased risk for PTSD, anxiety, depression, and substance abuse.

"But because the symptoms vary greatly among individuals, they do not point to a syndrome unique to these veterans. Unfortunately, because of the lack of objective predeployment health information, we do not have the baseline data needed to draw more definitive conclusions about many aspects of these veterans' long-term health," he said.

The idea that there is no unique Gulf War syndrome is "sort of a side issue," said Lea Steele, Ph.D., who is an epidemiologist at Kansas State University in Manhattan. Veterans continue to be sick and to have unexplained symptoms, said Dr. Steele, who is also the scientific director of the congressionally chartered Research Advisory Committee on Gulf War Veterans' Illnesses.

Currently, most veterans are being treated for their symptoms, but there have few treatment studies to date, she said. "The treatment area is an area that needs a lot of attention," Dr. Steele said.

Research in the area of veterans' multisymptom illnesses has been challenging, said Dr. Samuel J. Potolicchio, professor of neurology at George Washington University in Washington, and a member of the IOM committee that wrote the report.

Part of the problem is that the syndromes are ill defined and there is no test



A U.S. Marine patrol walks across the charred oil landscape near a burning well during perimeter security patrol near Kuwait City on March 7, 1991.

to diagnose these problems, he noted.

However, researchers at the VA have been working in this area and have produced a number of well-designed studies, he said. "It's unraveling little by little."

The IOM committee also found that:

- ▶ Deployment to the Gulf puts veterans at increased risk for posttraumatic stress disorder, anxiety, depression, and substance abuse.
- ▶ There does not appear to be an increase in the prevalence of peripheral neuropathy in deployed Gulf War veterans, compared with their nondeployed counterparts. This finding is based on history, physical examination, and electrophysiologic studies.

- ▶ There was no statistically significant difference in the rates of hypertension between deployed and nondeployed veterans in primary studies.

- ▶ Two studies have shown some evidence of an increased risk for birth defects in the

offspring of Gulf War veterans, but the studies have been difficult to interpret, according to the IOM report. Urinary tract abnormalities are the only set of defects that have been found in more than one well-designed study, the report said.

The IOM committee called on the VA and Department of Defense to conduct comprehensive pre- and postdeployment screening of health status, perform assessments of exposures during military deployments, and continue surveillance of adverse health outcomes. Surveillance is needed for a number of health outcomes including cancer, ALS, birth defects, adverse pregnancy outcomes, postdeployment psychiatric conditions, and mortality, according to the report. ■

The report—"Gulf War and Health, Volume 4: Health Effects of Serving in the Gulf War"—is available online at www.iom.edu or by calling 800-624-6242.

Alpha-Synuclein Gene Variation Associated With Parkinson's

BY MARY ANN MOON
Contributing Writer

Variations in the length of the alpha-synuclein gene promoter's dinucleotide repeat sequence have been linked to Parkinson's disease in a study analyzing DNA samples from more than 5,300 subjects around the world.

Mutations in the alpha-synuclein (SNCA) gene have been implicated before in Parkinson's disease (PD), but only within certain families and rarely among the general population.

"Our study demonstrates that the SNCA gene is not only a rare cause of autosomal dominant Parkinson disease in some families, but also a susceptibility gene for PD at the population level," reported Dr. Demetrius M. Maraganore of the Mayo Clinic, Rochester, Minn., and his associates.

"Based on our results, we estimate that REP1 [the alpha-synuclein gene promoter's dinucleotide repeat sequence] locus variability may explain approximately 3% of the risk in the gener-

al population," the researchers said (JAMA 2006; 296:661-70).

They used data from the Genetic Epidemiology of Parkinson's Disease Consortium to investigate SNCA gene mutations in what they described as "the largest case-control study of PD to date." The consortium collects and shares biospecimens and data collected at multiple sites worldwide.

For this study, DNA analysis was done on samples from 2,692 patients with PD and 2,652 unrelated control subjects.

Variability in the length of a dinucleotide repeat sequence within the SNCA promoter was found to be associated with PD susceptibility.

If further study finds that this risk is conferred via a mechanism of gene overexpression, interventions targeting SNCA expression may reduce the risk of developing PD in susceptible populations. It remains uncertain, however, whether therapies to reduce SNCA expression would affect the progression of existing PD, Dr. Maraganore and his associates noted. ■

Study Shows Strong Link Between RLS, Depression

SALT LAKE CITY — A strong relationship exists between restless legs syndrome and major depressive disorder, a community-based study suggests.

Of 42 patients with restless legs syndrome (RLS), approximately 21% had a lifetime diagnosis of major depressive disorder (MDD), compared with 8% of 982 control patients, for a 2.8 adjusted odds ratio for MDD risk. Patients participated in the Baltimore Epidemiologic Catchment Area study, Dr. Hochang B. Lee reported in a poster at the annual meeting of the Association of Professional Sleep Societies.

Participants completed a seven-item RLS questionnaire, and the National Institute of Mental Health Diagnostic Interview

Schedule was administered by a trained lay interviewer. Results were adjusted for relevant sociodemographic and health-related variables, noted Dr. Lee of the department of psychiatry at Johns Hopkins University, Baltimore.

The findings support those from a number of other studies in clinical samples, which also have suggested a relationship between depression and RLS, according to the investigator. Few studies, however, have focused on the link between MDD and RLS.

Future studies should focus on possible pathophysiologic mechanisms for the link between these common conditions, Dr. Lee concluded.

—Sharon Worcester