Gulf War and Health: Update of Health Effects of Serving in the Gulf War

Statement of

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and

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Board on the Health of Select Populations
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Committee on Veterans’ Affairs
U.S. House of Representatives

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Good morning Mr. Chairman and members of the subcommittee. My thanks to Congressman Mitchell and members of the Subcommittee on Oversight and Investigations, House Committee on Veterans’ Affairs for your concern regarding Gulf War veterans’ health.

My name is Stephen Hauser. Since 1992, I have served as professor and chair of the Department of Neurology at the University of California, San Francisco. I am trained in internal medicine, neurology, and immunology. I am also an elected member of the Institute of Medicine. I am here today because I served as Chair of the committee that worked on the Institute of Medicine (IOM) report *Gulf War and Health: Update of Health Effects of Serving in the Gulf War*. The sponsor of the study was the Department of Veterans Affairs (VA). The report was released to the VA and Congress on April 8<sup>th</sup> of this year.

I will focus on three main topics in my testimony. First, I will briefly discuss the overall IOM study process followed by the committee in developing our report and the committee’s approach to its charge, including the process the committee used to draw its conclusions regarding the association between deployment to the Gulf War and specific health outcomes. Second, I will summarize our specific findings and conclusions. And finally, I present the committee’s recommendations for future research to help address the continuing health concerns of Gulf War veterans.

The IOM is a part of The National Academies, a private, non-governmental organization that provides independent scientific-based advice to policymakers and the public. Among the IOM’s signature products is the consensus report produced by expert individuals from universities, nonprofit organizations, and other types of organizations. The long established study process, followed throughout the Academies, ensures that committee members are
balanced for any biases and free from actual or potential conflicts of interest. Additionally, during committee meetings and deliberations, there is no sponsor oversight; the sponsoring organization does not participate in any portion of the preparation and review of the IOM report. In instances when the committee requests information from the sponsor, those materials are made publicly available. After the committee develops a draft consensus report based on a detailed review of available literature, hearing from additional experts, and internal deliberation, the draft report undergoes a formal external peer-review process. The reviewers are anonymous to the committee and IOM staff. They are asked to read the report and provide comments on whether the committee has addressed its charge, the strength of the evidence for and the validity of the committee’s conclusions, and clarity and flow of the report. All reviewer comments must be addressed by the committee and the report must be approved by The National Academies Report Review Committee before it can be released to the study sponsor and the public.

The current report is an update of the 2006 report *Gulf War and Health, Volume 4: Health Effects of Serving in the Gulf War*. It examines the relevant literature published since 2005, the time of the last literature search for the 2006 report, on the health of veterans related to deployment to the Persian Gulf in 1990-1991. As requested by the VA, the specific charge to our update committee was to review, evaluate, and summarize the literature on the following health outcomes that were noted in the 2006 report as having high incidence or prevalence in the Gulf War deployed veterans: cancer (particularly brain and testicular cancer), amyotrophic lateral sclerosis (ALS) and other neurologic diseases (such as Parkinson’s disease and multiple sclerosis), birth defects and other adverse pregnancy outcomes, and post-deployment psychiatric conditions. In addition, and as recommended by the 2006 report, the committee also reviewed studies on cause-specific mortality in Gulf War veterans.
The committee initially examined over 1000 potentially relevant references from peer-reviewed publications for the *Update* report. After an assessment of the titles and abstracts, 400 of these references were considered particularly relevant and thus reviewed in depth by the committee. In addition, to ensure a comprehensive approach, all the epidemiologic studies included in *Volume 4* were also reviewed by this committee in order to draw conclusions about the strength of association between deployment to the Gulf War and particular health outcomes. The committee held two public sessions where interested parties, such as representatives from veteran-service organizations and Gulf War veterans, were invited to speak. As requested by VA Secretary Shinseki, the committee also invited representatives from the VA Research Advisory Committee of Gulf War Veterans’ Illness (RAC) to present the findings and conclusions from their report, *Gulf War Illness and the Health of Gulf War Veterans: Scientific Findings and Recommendations*, which was published in November 2008.

In order to draw conclusions on the strength of the evidence for an association between deployment to the Gulf War and a health outcome, the committee used categories of association. The following five categories are long established and have been used by previous Committees on Gulf War and Health and other IOM committees evaluating topics such as vaccine safety and Agent Orange. They are widely accepted by and familiar to Congress, the VA, and veteran groups. The categories are:

- Sufficient evidence of a causal relationship, that is, the evidence is sufficient to conclude that between being deployed to the Gulf War causes a health outcome.
- Sufficient evidence of an association; that is, a positive association has been observed between deployment to the Gulf War and a health outcome in humans.
• Limited/suggestive evidence of an association; that is, some evidence of an association between deployment to the Gulf War and a health outcome in humans exists.

• Inadequate/insufficient evidence to determine whether an association exists; that is, available studies are of insufficient quality, validity, consistency or statistical power to permit a conclusion regarding the presence or absence of an association.

• And finally, limited/suggestive evidence of no association; that is, several adequate studies are consistent in not showing an association between deployment and a health outcome.

In order to reach consensus and determine the category of association assigned for each health outcome, the committee took a weight-of-the-evidence approach based on the studies and their classification as primary or secondary.

Listed below is a box summarizing the committee’s findings. Sufficient evidence was found to conclude that a casual relationship exists between being deployed to the Gulf War and posttraumatic stress disorder (PTSD)—the only outcome placed in this category. Also of note, sufficient evidence suggests an association exists between deployment to the Gulf War and the following health outcomes: other psychiatric disorders, including generalized anxiety disorder, depression, and substance abuse, particularly alcohol. These psychiatric outcomes can persist for at least 10 years post deployment. Sufficient evidence of an association was also seen for gastrointestinal (GI) symptoms that are consistent with functional GI disorders such as irritable bowel syndrome and functional dyspepsia; for multi-symptom illness; and for chronic fatigue syndrome.
Summary of Findings Regarding Associations Between Deployment to the Gulf War and Specific Health Outcomes

**Sufficient Evidence of a Causal Relationship**

- PTSD.

**Sufficient Evidence of an Association**

- Other psychiatric disorders, including generalized anxiety disorder, depression, and substance abuse, particularly alcohol abuse. These psychiatric disorders persist for at least 10 years after deployment.
- Gastrointestinal symptoms consistent with functional gastrointestinal disorders such as irritable bowel syndrome and functional dyspepsia.
- Multisymptom illness.
- Chronic fatigue syndrome.

**Limited/Suggestive Evidence of an Association**

- ALS.
- Fibromyalgia and chronic widespread pain.
- Self-reported sexual difficulties.
- Mortality from external causes, primarily motor-vehicle accidents, in the early years after deployment.

**Inadequate/Insufficient Evidence to Determine Whether an Association Exists**

- Any cancer.
• Diseases of the blood and blood-forming organs.
• Endocrine, nutritional, and metabolic diseases.
• Neurocognitive and neurobehavioral performance.
• Multiple sclerosis.
• Other neurologic outcomes, such as Parkinson’s disease, dementia, and Alzheimer’s disease.
• Incidence of cardiovascular diseases.
• Respiratory diseases.
• Structural gastrointestinal diseases.
• Skin diseases.
• Musculoskeletal system diseases.
• Specific conditions of the genitourinary system.
• Specific birth defects.
• Adverse pregnancy outcomes such as miscarriage, stillbirth, preterm birth, and low birth weight.
• Fertility problems.

**Limited/Suggestive Evidence of No Association**

• Peripheral neuropathy.
• Mortality from cardiovascular disease in the first 10 years after the war.
• Decreased lung function in the first 10 years after the war.
• Hospitalization for genitourinary diseases.
I would like to elaborate a bit more on how the committee evaluated “multi-symptom illness”, also referred to as Gulf War illness or Gulf War syndrome. Numerous studies have documented that those deployed to the Gulf War have an increased prevalence of a disabling complex of self-reported symptoms such as fatigue, musculoskeletal pain, sleep disturbances, cognitive dysfunction, and moodiness, among others. The Volume 4 committee looked at this symptom reporting by deployed Gulf War veterans and attempted to determine whether a unique illness could be defined by these symptoms but our committee accepted that multi-symptom illness was indeed a diagnostic entity and examined the literature to make conclusions regarding its association with deployment to the Gulf War. We did not attempt to determine if the multisymptom illness seen in Gulf War veterans was a disease unique to them.

Research has identified an association between self-reported multi-symptom illness and self-reported exposures to several chemicals that inhibit cholinesterase, an enzyme that is important for proper functioning of the nervous system. Pyridostigmine bromide (PB) is one example of a cholinesterase inhibitor as are many pesticides. In the appendix to our report, the committee described how Gulf War veterans may have been exposed to cholinesterase inhibitors, including evidence potentially linking these exposures to multi-symptom illness. After careful examination of both animal studies and human studies, the committee concluded that there was insufficient evidence to link possible exposures to cholinesterase-inhibiting chemical agents to the multi-symptom illness seen in Gulf War veterans.

The committee believes the path forward for Gulf War veterans consists of two branches, and has made recommendations accordingly. First, as with numerous other Gulf War and Health
reports, the committee calls for improved studies of Gulf War veterans that are designed and conducted to more accurately characterize deployment and potential related adverse environmental influences, and that address possible confounding factors, such as smoking. However, the committee feels that further studies based solely on self-reports may not contribute to the scientific evidence or accurately reconstruct exposures that occurred 20 years ago in the Persian Gulf. The committee recognizes that establishing Gulf War veterans’ physical and mental health baseline status is a challenge. Robust cohorts need to be followed to track the development of ALS, MS, brain cancer, psychiatric conditions, and other health problems, such as cancers, cardiovascular disease, and neurodegenerative diseases that manifest later in life. Some large, well-characterized cohorts have already been established, such as the US cohort studied by the VA, the two UK cohorts, and the Australian cohort. In the future, these cohorts might provide information on diseases with low prevalence, such as ALS and brain cancer.

The committee also recommends a second major branch of inquiry regarding the effort to further define the diagnosis of and develop effective treatments for multisymptom illness. As our understanding of genetics, molecular science, and brain imaging expand, it should be possible to carry out large-scale, well-designed studies to identify the differences in veterans with persistent medical symptoms as compared to their healthy deployed counterparts. These differences include genetic variants; molecular profiles of gene expression; markers such as changes in DNA structure as a result of exposures to chemicals or viruses; immune system activation; and changes in the brain. The committee believes that useful biomarkers may be indentified to help diagnose and treat unexplained symptoms such as chronic fatigue, muscle and joint pain, sleep disturbance, difficulty in concentration, and depression.
Finally, the committee believes it would be valuable to undertake high quality clinical trials that may result in identifying effective, evidence-based treatments for multisymptom illness. In short, with the progress in scientific capabilities, well organized efforts to accurately diagnosis and clinically treat multisymptom illness and other unexplained illnesses would be most valuable to help our suffering veterans.

On behalf of the Committee on *Gulf War and Health: Health Effects of Serving in the Gulf War, Update 2009*, I thank you for your trust in our ability to assist with your important work on veterans’ health and for asking me to testify before this subcommittee. I look forward to answering any questions you may have.
Stephen L. Hauser, M.D. (Committee Chair)

Dr. Hauser is Professor and Chair of the Department of Neurology at the University of California, San Francisco. He is board certified in both internal medicine and neurology. He has been President, American Neurological Association and received the 2008 John Dystel Prize for Multiple Sclerosis Research. He is as Editor-in-Chief of the journal Annals of Neurology and is also an editor of the textbook Harrison’s Principles of Internal Medicine. His research interests are in the areas of multiple sclerosis, neuroimmunology, autoimmunity, and human genetics. Dr. Hauser is a member of the Institute of Medicine and has served on the IOM Membership Committee and on the Committee on Multiple Sclerosis: Current Status and Strategies for the Future. Dr. Hauser was also recently appointed to the The Presidential Commission for the Study of Bioethical Issues. He received his M.D. from the Harvard Medical School.