GULF WAR AND HEALTH

Statement of

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Update of Health Effects of Serving in the Gulf War
Board on the Health of Select Populations
Institute of Medicine
The National Academies of Sciences, Engineering, and Medicine

before the

Subcommittee on Oversight and Investigations
Committee on Veterans Affairs
U.S. House of Representatives

February 23, 2016

Good morning, Chairman Miller, Ranking Member Kuster, and members of the Committee. My name is Deborah Cory-Slechta. I am a Professor of Environmental Medicine, Pediatrics and Public Health Sciences, and Acting Chair of the Department of Environmental Medicine at the University of Rochester School of Medicine. I served as the Chair of the Committee on Gulf War and Health, Volume 10: Update of Health Effects of Serving in the Gulf War of the National Academies of Sciences, Engineering, and Medicine. The National Academy of Sciences was chartered by Congress in 1863 to advise the government on matters of science and technology and later expanded to include the National Academies of Engineering and Medicine.

The Institute of Medicine (IOM), part of the National Academies of Sciences, Engineering, and Medicine, released its 10th report on Gulf War and Health on February 11 of this year. The committee that I chaired was asked to review and evaluate the scientific and medical literature regarding associations between illness and exposure to toxic agents, environmental or wartime hazards, or preventive medicines or vaccines associated with Gulf War service and to pay particular attention to neurological disorders (e.g., Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, and migraines), cancer (especially brain cancer and lung cancer), and chronic multisymptom illness (also known as Gulf War illness). Volume 10 updated two earlier Gulf War and Health reports, Volume 4, published in 2006, and Volume 8 published in 2010. The committee made recommendations for future research on Gulf War veterans. I should note that the committee was composed of experts in neurology, epidemiology, pain, psychiatry, neurocognitive disorders, environmental health and toxicology; and clinicians and researchers, none of whom received funding from Gulf War illness research programs.

For the most part, the Volume 10 committee followed the approach used by earlier committees. It held two public sessions at which it heard from representatives of VA, several Gulf War veterans and veteran service organizations, Gulf War researchers, and representatives of the VA Research Advisory Committee on Gulf War Veterans' Illnesses. The committee did not address policy issues, such as service connection, compensation, or the cause of or treatment for Gulf War illness. The committee conducted an extensive literature search and reviewed the Volumes 4 and 8 primary and secondary epidemiologic studies and the conclusions reached by those committees. Other types of studies—such as animal toxicology, neuroimaging, and genetics—were also considered.

Primary studies had to be published in a peer-reviewed journal or other rigorously peer-reviewed publication; demonstrate rigorous methods (for example, have an appropriate control group and include adjustments for confounders); include information on a persistent (not acute) health outcome; use appropriate laboratory testing, if applicable; and have a study population that was generalizable to and representative of the Gulf War veteran population. Secondary studies were those studies that did not necessarily meet all the criteria of a primary study. Many of the secondary studies relied on self-reports of various diagnoses rather than an examination by a health professional or a medical record review.

The committee used the same categories of association relating health conditions to Gufl War deployment as used by previous Gulf War and Health and other IOM committees that have evaluated scientific literature, that is:

- Sufficient Evidence of a Causal Relationship
- Sufficient Evidence of an Association
- Limited/Suggestive Evidence of an Association

- Inadequate/Insufficient Evidence to Determine Whether an Association Exists
- Limited/Suggestive Evidence of No Association

The committee found that in spite of the many millions of dollars that have been spent on researching the health of Gulf War veterans there has been little substantial progress in our understanding of their health, particularly of Gulf War illness. The Volume 10 committee found little evidence to warrant changes to the Volume 8 conclusions regarding the strength of the association between deployment to the Gulf War and adverse health outcomes. Veterans who were deployed to the Gulf War do not appear to have an increased risk for many long-term health conditions with the exceptions of PTSD, Gulf War illness, chronic fatigue syndrome, functional gastrointestinal conditions, generalized anxiety disorder, depression, and substance abuse. The committee's conclusions are briefly summarized in the Box 1.

BOX 1
Summary of Conclusions Regarding Associations Between Deployment to the Gulf War and Specific Health Conditions

Sufficient Evidence of a Causal Relationship
- Posttraumatic stress disorder (PTSD)

Sufficient Evidence of an Association
- Generalized anxiety disorder, depression, and substance abuse (particularly alcohol abuse)
- Gastrointestinal symptoms consistent with functional gastrointestinal disorders such as irritable bowel syndrome and functional dyspepsia
- Chronic fatigue syndrome
- Gulf War illness

Limited/Suggestive Evidence of an Association
- Amyotrophic lateral sclerosis (ALS)
- Fibromyalgia and chronic widespread pain
- Self-reported sexual difficulties

Inadequate/Insufficient Evidence to Determine Whether an Association Exists
- Any cancer
- Cardiovascular conditions or conditions of the blood and blood-forming organs
- Endocrine, nutritional, and metabolic conditions
- Neurodegenerative diseases other than ALS
- Neurocognitive and neurobehavioral performance

- Migraines and other headache disorders
- Other neurologic conditions
- Respiratory conditions
- Structural gastrointestinal conditions
- Skin conditions
- Musculoskeletal system conditions
- Genitourinary conditions
- Specific birth defects
- Adverse pregnancy outcomes (e.g., miscarriage, stillbirth, preterm birth, and low birth weight)
- Fertility problems
- Increased mortality from any cancer, any neurologic disease (including multiple sclerosis, Alzheimer's disease, Parkinson's disease, and ALS), respiratory disease, or gastrointestinal disease

Limited/Suggestive Evidence of No Association

- Objective measures of peripheral neurologic conditions
- Multiple sclerosis
- Mortality from cardiovascular, infectious, or parasitic diseases
- Decreased lung function
- Mortality due to mechanical trauma or other external causes

As requested in its statement of task, the committee had additional discussions pertaining to Gulf War illness, neurologic conditions, and lung and brain cancer on those health conditions and other aspects of Gulf War veteran health.

Gulf War Illness. Gulf War illness is the signature adverse health outcome of having served in the Persian Gulf region. Multiple studies found that some Gulf War veterans, regardless of their country of origin and their different deployment-related exposures, have persistent, debilitating, and varying symptoms (such as joint and muscle pain, fatigue, and cognitive problems) of Gulf War illness. In spite of over 2 decades of research to define, diagnose, and treat Gulf War illness, little progress has been made in elucidating the pathophysiologic mechanisms that underlie it, the exposures that may have caused it, or treatments that are generally effective for it.

Gulf War illness is not an easily defined or diagnosed condition. The committee concluded that it is not a psychosomatic illness, but it does present with diverse symptoms, many of which overlap with other health conditions such as chronic fatigue syndrome,

neurodegenerative disorders, and musculoskeletal problems. Based on available research data, it does not appear that a single mechanism can explain the multitude of symptoms seen in Gulf War illness, and the committee found it unlikely that a single definitive causal agent would be identified this many years after the war. Furthermore, most Gulf War illness studies have excluded the psychological aspects of the condition with regard to both diagnosis and treatment although veterans report symptoms such as chronic pain and sleep disturbances that may be amenable to psychological therapies, alone or in conjunction with other treatments.

The committee concluded that although the existence of an animal model would be advantageous for identifying and evaluating treatment strategies for Gulf War illness, it cautions that developing such an animal model is precluded by the absence of any objective measures of chemical and nonchemical exposures during Gulf War service, let alone the frequency, duration, or dose of those exposures, or the highly likely interactive effects of multiple exposures.

Neurologic Conditions. The committee found little new information pertaining to multiple sclerosis, Parkinson's disease, Alzheimer's disease, or migraines. ALS is the only neurologic disease for which the committee found limited/suggestive evidence for an association with deployment to the Gulf War. The committee concluded that further follow-up of this uniformly fatal disease is warranted. The Gulf War veteran population is still young with respect to the development of other neurodegenerative diseases; therefore, the effects of deployment on their incidence and prevalence may not yet be obvious.

Lung Cancer and Brain Cancer. The committee found the evidence for brain cancer to be inadequate/insufficient and it found no statistically significant increase in the current risk of brain cancer in deployed Gulf War veterans compared with their nondeployed counterparts. This finding is mirrored in another recent IOM study. With regard to lung cancer, the committee notes

that the 10-15 years of follow-up that have been reported may not have been adequate to account for the long latency of this disease. Although one new study found an increased incidence of lung cancer for deployed versus nondeployed veterans, neither veteran group had a greater risk when compared with the general population, and the study did not indicate smoking status. Thus, the committee found that the evidence continues to be inadequate/insufficient to determine whether deployed Gulf War veterans are at increased risk of having any cancer, including lung and brain cancer. The relative rarity of cancers such as brain cancer argues for larger studies with adequate power to detect them.

Other Health Outcomes. The committee finds that sufficient time has elapsed to determine that Gulf War deployed veterans do not have an increased incidence of circulatory, hematologic, respiratory, musculoskeletal, structural gastrointestinal, genitourinary, reproductive, or chronic skin conditions compared with their nondeployed counterparts. **A**s Gulf War veterans age, it will be more difficult to differentiate the effects of deployment from the natural effects of aging on morbidity and mortality. Furthermore, the association of deployment to the Gulf War with PTSD, anxiety disorders, substance abuse, and depression is well established, and further studies to assess whether there is an association are not warranted.

Although there are well-known differences in disease profiles according to sex and race/ethnicity, few studies on Gulf War veterans specifically report outcomes for women or minorities, although many veteran studies adjust for sex and race/ethnicity in their analyses. This lack of distinction is important and makes it imperative that researchers report sex-specific and race/ethnicity-specific outcomes, particularly in large cohorts and where population subgroups may be oversampled.

In conclusion, what is striking about this and prior Gulf War and Health committees' findings is that the health conditions found to be associated with Gulf War deployment are primarily functional medical disorders such as Gulf War illness and irritable bowel syndrome, and mental health disorders such as PTSD and depression. What links these conditions is that they have no objective medical diagnostic tests and are diagnosed based on subjective symptom reporting.

To be clear, the committee recognizes that Gulf War illness is a distinct medical condition with symptoms that affect many organs and organ systems including the brain; these symptoms include cognitive difficulties, memory problems, and headaches. Many other chronic illnesses from kidney disease to cancer also can affect the brain.

Based on its conclusions regarding the association between deployment to the Gulf War and the health conditions seen in Gulf War veterans 25 years after the war, the committee made the following recommendations:

- **Recognize the connections and complex relationships between brain and physical functioning and should not exclude any aspect of Gulf War illness with respect to improving its diagnosis and treatment.**
- **The Department of Veterans Affairs and the Department of Defense should develop a joint and cohesive strategy on incorporating emerging diagnostic technologies and personalized approaches to medical care into sufficiently powered future research to inform studies of Gulf War illness and related health conditions.**
- **The Department of Veterans Affairs should continue to conduct follow-up assessments of Gulf War veterans for neurodegenerative diseases that have long latencies and are**

associated with aging; these include amyotrophic lateral sclerosis, Alzheimer's disease, and Parkinson's disease.

- **The Department of Veterans Affairs should conduct further assessments of cancer incidence, prevalence, and mortality because of the long latency of some cancers. Such studies should maximize the use of cancer registries and other relevant sources, data, and approaches, and should have sufficient sample sizes to account for relatively rare cancers and to be able to report sex-specific and race/ethnicity-specific information.**
- **Further studies to assess the incidence and prevalence of circulatory, hematologic, respiratory, musculoskeletal, structural gastrointestinal, genitourinary, reproductive, endocrine and metabolic, chronic skin, and mental health conditions due to deployment in the Gulf War should not be undertaken. Rather, future research related to these conditions should focus on ensuring that Gulf War veterans with them receive timely and effective treatment.**
- **Without definitive and verifiable individual veteran exposure information, further studies to determine cause-and-effect relationships between Gulf War chemical exposures and health conditions in Gulf War veterans should not be undertaken.**
- **Sex-specific and race/ethnicity-specific health conditions should be determined and reported in future studies of Gulf War veterans. In addition, selected prior studies (e.g., large cohort studies) should be reviewed to determine whether reanalysis of the data to assess for possible sex-specific and race/ethnic-specific health conditions is feasible.**
- **Future Gulf War research should place top priority on the identification and development of effective therapeutic interventions and management strategies for Gulf War illness. The Department of Veterans Affairs should support research to determine**

how such treatments can be widely disseminated and implemented in all health care settings.

The committee believes that it is time that research efforts move forward and focus on improving treatment and medical management of veterans for Gulf War illness, including all affected organs and systems of the body. Further exploration of treatments and management strategies for the symptoms of Gulf War illness, even in the absence of a definitive etiology, is warranted.

Finally, the committee wants to emphasize that it did not recommend that research on the health of Gulf War veterans be stopped. Rather, the committee found that research that continues to seek a causal link between Gulf War illness or other health conditions found in Gulf War veterans and specific chemical exposures, such as PB, sarin, or pesticides, is not likely to yield useful information. Many millions of dollars have been spent on this research with few tangible results and those resources are more likely to have an impact if focused on treatment and management strategies for these veterans.

Thank you and I am pleased to answer any questions that you may have.