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Gulf War & Health Volume 10

Update of Health Effects of Serving
in the Gulf War, 2016

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COMMITTEE ON GULF WAR AND HEALTH, VOLUME 10: UPDATE OF HEALTH EFFECTS OF SERVING IN THE GULF WAR

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Statement of Task

- The IOM will comprehensively review, evaluate, and summarize the available scientific and medical literature regarding health effects in the 1990-1991 Gulf War veterans.
- Update earlier IOM reviews of Gulf War and Health, particularly Volume 4 (2006) and Volume 8 (2010)
- Provide recommendations for future research efforts on Gulf War veterans
- The committee will 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 [Gulf War illness].

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Committee's Approach

- Held two public sessions to hear from VA, VSOs, individual veterans, and Gulf War researchers
- Heard presentations from representatives of the VA Research Advisory Committee on Gulf Veterans' Illness on 2014 report
- Conducted extensive literature searches
- Reviewed literature from new searches as well as literature cited in Volumes 4 and 8
- As a group, reviewed each study critically to determine if it met criteria for primary or secondary study
- Discussed the entire data set for each health outcome in plenary session and reached consensus as to the category of association to be assigned to that health outcome using a weight of the evidence approach

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Primary and Secondary Studies

Committee looked at both primary and secondary studies:

- Primary studies had robust methods, included some type of medical evaluation and were considered to be representative of the Gulf War veteran population
- Secondary studies did not meet the criteria for primary studies

Other Relevant Studies were those that did not directly assess exposure-outcome relationship but were considered to be important for context and related research

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General Observations

- Few new primary studies
- Studies rarely reported outcomes in women or minorities
- Associations between Gulf War service and health conditions are generally the same as Vol. 8

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Sufficient Evidence of a Causal Relationship

Evidence is sufficient to conclude that a causal relationship exists between being deployed to the Gulf War and a health outcome.

- Posttraumatic stress disorder (PTSD)

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Sufficient Evidence of an Association

Evidence suggests an association, in that a positive association has been observed between deployment to the Gulf War and a health outcome in humans; however there is some doubt as to the influence of chance, bias, and confounding.

- 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

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Limited/Suggestive Evidence of an Association

Some evidence of an association between deployment to the Gulf War and a health outcome in humans exists, but this is limited by the presence of substantial doubt regarding chance, bias, and confounding.

- Amyotrophic lateral sclerosis (ALS)
- Fibromyalgia and chronic widespread pain
- Self-reported sexual difficulties

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Inadequate/Insufficient Evidence to Determine Whether an Association Exists

The available studies are of insufficient quality, validity, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association between deployment to the Gulf War and a health outcome in humans.

- Any cancer
- Neurodegenerative diseases other than ALS (e.g., Parkinson's disease)
- Neurocognitive and neurobehavioral performance
- Migraines/headache disorders
- Other neurologic outcomes
- Cardiovascular conditions
- Endocrine and metabolic conditions
- Respiratory diseases

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Inadequate/Insufficient Evidence (cont)

- Structural gastrointestinal diseases
- Skin conditions
- Musculoskeletal system diseases
- 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 MS, Alzheimer's disease, Parkinson's disease, and ALS), respiratory disease, or gastrointestinal disease

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Limited/Suggestive Evidence of No Association

Several adequate studies, covering the full range of levels of exposure that humans are known to encounter, are consistent in not showing an association between deployment and a health outcome. This conclusion is inevitably limited to the conditions, levels of exposure, and length of observation covered by the available studies; the possibility of a very small increase in risk at the levels of exposure studied can never be excluded.

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

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Animal Studies

The committee's review of animal studies focused on papers that assessed multiple chemical and other exposures (e.g., exposure to PB, pesticides, and stress at the same time or in close succession).

- Our ability to draw conclusions was limited by variation in methods, exposures, and outcomes measured
- No replication of findings
- Inconsistent results
- Little reliable information on actual Gulf War exposures

Conclusions:

- Animal studies have not been successful in suggesting a mechanism by which deployment exposures during the Gulf War might lead to Gulf War Illness.
- Development of an animal model of Gulf War illness may not be possible.

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Gulf War Illness

- Gulf War illness is not a psychosomatic illness but many GW illness symptoms (e.g., fatigue, GI problems) are shared by psychological conditions such as depression or PTSD, but most studies have excluded the psychological aspects of Gulf War illness.
- No single mechanism explains the multitude of symptoms seen in Gulf War illness.
- Unlikely that a single definitive causal agent will be identified this many years after the war.
- Gulf War illness affects multiple organ systems: brain, gut, heart, liver, immune system, thyroid, adrenals, pituitary, gonads, bone, and skin.
- Future research should acknowledge interconnectedness of brain and body for treatment. To ignore this is a disservice to veterans.

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Gulf War Illness: Recommendations

- Any future studies of Gulf War illness should include the connections and complex relationships between brain and physical functioning, as we do for other diseases, and should not exclude any aspect of the illness with regard to improving its diagnosis and treatment.
- VA and DoD 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.
- Biomonitoring during future conflicts (individual and environmental) will be essential for helping to determine chemical exposures and any resulting health conditions.

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Gulf War Illness: Recommendations

Top priority should be the identification and development of effective therapeutic interventions and management strategies for Gulf War illness.

This research on treatments and strategies should address all affected organs and systems of the body. Such research is warranted even in the absence of a definitive etiology.

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Neurologic Conditions

- Little new information pertaining to multiple sclerosis, Parkinson's disease, Alzheimer's disease, or migraines.
- Limited/suggestive evidence of association of deployment with developing ALS, but no association with ALS mortality (a uniformly fatal disease); thus, further follow-up is warranted.
- GW veterans are still young for development of other neurodegenerative diseases; therefore, deployment effects on their incidence and prevalence may not yet be obvious.

Recommendation:

- Thus, VA should continue to conduct follow-up assessments of Gulf War veterans for those neurodegenerative diseases that have long latencies and are associated with aging; e.g., ALS, Alzheimer's disease, and Parkinson's disease.

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Lung and Brain Cancer

- GW veterans are not at increased risk for cancer 10–15 years after the war but many cancers have longer latencies.
- New studies found no increase in brain cancer risk; one study found increased incidence of lung cancer in GW deployed veterans but veterans had no greater risk of lung cancer than the general population (smoking status not reported).
- Rare cancers, such as brain cancer, require studies with adequate power to detect them by pooling data and using a variety of data sources such as state cancer registries.

Recommendation:

- VA should conduct further assessments of cancer incidence, prevalence, and mortality due to long latency of some cancers; studies should use cancer registries and a variety of data sources, have sufficient sample sizes to detect rare cancers, and report sex-specific and race/ethnicity-specific information.

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Other Health Conditions

- GW veterans do not have an increased incidence of circulatory, hematologic, respiratory, musculoskeletal, gastrointestinal, genitourinary, reproductive, and chronic skin conditions compared with their nondeployed counterparts.
- As GW veterans age, it will be more difficult to differentiate the effects of deployment from the natural effects of aging on morbidity and mortality.
- There are no data on the delayed effects of Gulf War exposures, such as nerve agents and PB, to indicate that such toxicants would remain in the body and would be able to cause disease this long after the Gulf War.
- With the exception of diseases with long latency periods such as cancer, it is not reasonable to expect increased risks of diseases associated with Gulf War toxic exposures now.
- Because the association of deployment to the Gulf War with PTSD, anxiety disorders, substance abuse, and depression is well established, further studies to assess whether there is an association are not warranted.

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Additional Recommendations for Future Research

- Without definitive and verifiable chemical exposure information, further studies to determine cause-and-effect relationships between Gulf War 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/ethnicity-specific health conditions is feasible.

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