

25 Years after the Gulf War: Gulf War Illness, Brain Cancer and Future Research

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On this week marking the 25th anniversary of the Gulf War, I would like to express my concern and disappointment with the conclusions from the recent volume 10 Institute of Medicine Gulf War Report and highlight some of the important research that is ongoing in this field.

Gulf War Illness

GWI is a constellation of chronic health symptoms including fatigue, pain, headaches, gastrointestinal and cognitive problems. It is a multi-system disorder meaning that it affects not only the central nervous system but also the immune and gastrointestinal systems. It affects about a third of the nearly 700,000 veterans deployed to the war.

Gulf War Illness as a Functional Disorder

The IOM report goes to great length to describe GWI as a self-reported symptom based disorder for which there are no current objective biomarkers and therefore it must be a 'functional disorder' meaning it has no physical cause. The report describes it to be similar to other well accepted symptom based disorders including post-traumatic stress disorder (PTSD). In fact, this report places PTSD as the only disorder that has 'sufficient evidence of causal association' to deployment to the Gulf War while it places GWI in the second category of 'sufficient evidence of an association' to deployment to the Gulf War.

However, less than 10% of GW veterans have been diagnosed with PTSD and more than 30% have been diagnosed with GWI. In addition, it is completely unclear why GWI is not also causally-related to deployment to the war when both disorders are diagnosed the same way – by self-report of chronic health symptoms.

The report also stresses that the health conditions associated with Gulf War deployment are primarily mental health disorders and functional medical disorders and that these associations emphasize the interconnectedness of the brain and body.

However, the brain and body are interconnected in GWI not because this is a stress-related disorder without a unifying pathobiological cause as the IOM report suggests, but rather because they are all part of the brain and immune pathways

that are activated as part of the neuroinflammatory response to pesticide and nerve agent exposures. These chemicals directly target the nervous system and cause inflammation. These pathways start by activating the immune cells in the brain called microglia that release chemical messengers called cytokines in the brain and the many body systems that are affected in GWI. Activating these inflammatory systems in the brain and throughout the body can result in chronic symptoms such as joint and muscle pain, memory problems, fatigue, headaches, and gastrointestinal distress—all symptoms found in GWI. Researchers call this type of chronic condition a post-inflammatory brain syndrome.

In fact, a paper by Gulf War researchers from the Centers for Disease Control (CDC) recently showed that Gulf War-relevant pesticides and nerve agents produced a neuroinflammatory response resulting in hundreds-fold higher cytokine chemical signaling in a GWI animal model. Preliminary studies in veterans with GWI suggest increased cytokine levels that correlate with GWI symptoms as well.

Treatment focus for Veterans with GWI

The IOM report has concluded that research efforts should be realigned to focus on the treatment and ‘management’ of Gulf War illness rather than its causes. However, biological targets focused on neuroinflammatory markers described above provide tangible and targeted treatment strategies for GWI. Researchers at Boston University, Nova Southeastern University and VA medical centers in Boston, Bronx and Miami are currently assessing the effectiveness of targeted treatment trials using intranasal insulin, D-cycloserine and Co-enzyme Q10 to treat the constellation of symptoms in GWI including cognitive, fatigue and pain symptoms. Clinical researchers can do better for our veterans than ‘manage’ their symptoms as the IOM suggests and the research community is hopeful that these currently funded treatments will provide much needed symptom relief for ill Gulf War veterans.

Brain Cancer Association with Gulf War Service

The IOM report also states that the results of two published VA studies reporting significantly increased brain cancer mortality rates found in GW veterans who were in close proximity to the Khamisiyah weapons depot detonations where large stores of sarin/cyclosarin were destroyed cannot be trusted because the exposure plume modelling done to determine who was exposed may be inaccurate. However, inaccuracies in exposure modeling often make the analysis less sensitive rather than more sensitive to finding differences between groups. Therefore, finding a 2 and 3 fold increase in brain cancer deaths in sarin exposed GW veterans suggests that these rates are likely an underestimate of effect rather than an overestimate of the effect of sarin exposure on brain cancer mortality in GW veterans.

Conclusion

The IOM report has downplayed the importance of continuing to research the remaining questions in GWI including identifying biomarkers of current illness, prior neurotoxicant exposures and targeted treatment strategies. This work is critically important to Gulf War veterans who suffer from chronic health effects from these toxicant exposures but also for many others including those who are occupationally exposed to pesticides, including farmers and pesticide applicators around the world. Gulf War veterans are counting on researchers to identify the cause and pathobiology of their debilitating illness, and to identify treatments that will work to improve all of their symptoms, not just manage them.

Most importantly, the end result of this report is that GW veterans suffering from brain cancer or family members of those who have already succumbed to brain cancer will not receive VA benefits now or likely ever for their service-related mortality. These veterans have been forced to fight for benefits while they are fighting for their lives. These veterans should be given the benefit of the doubt in providing them with VA service connection for this service-related mortality.