

LETTER TO THE EDITOR

THE MYSTERY OF GULF WAR SYNDROME PERSISTS

Gulf War Syndrome (GWS), also known as Gulf War Illness (GWI), is a long-term multi-symptom disorder which was described in military veterans and civilian workers who were employed in the first Gulf War (1990–1991). Out of approximately 700 000 soldiers who served in Operation Desert Storm (ODS), one-fourth to one-third (25–32%) of them reported symptoms corresponding to GWS. Medically unexplained symptoms have been reported among both civilians and military personnel involved in the combat. A wide range of acute and chronic symptoms have been linked to it, including fatigue, muscle pain, cognitive problems, rashes and diarrhea. Twenty-five years after the end of the fighting, the mystery of GWS persists.

During the war, personnel were exposed to a wide variety of known and potential health hazards. These potential exposures include smoke from oil well fires, nerve agents, extreme hot and cold weather, petroleum products and fumes, pesticides, depleted uranium, endemic infectious diseases and other physical and psychological stressors. Furthermore, prophylactic approaches such as immunization against anthrax and botulism, and the use of the nerve agent protection pill – pyridostigmine bromide (PB pill) – are often discussed as potential causes of GWS (Iversen et al., 2007).

But the GWS is still difficult to define and diagnose, and there is no broad agreement on the diagnostic criteria, let alone an exact cause. Commonly reported symptoms include pain, fatigue, mental fog, memory problems, headaches, insomnia, and gastrointestinal problems. Over two decades, scientists have argued whether the GWS is a real syndrome or just “an unspecific reaction to the stress occurring at war” (GWH, 2010). Many studies have been carried out and much money has been spent to unravel this problem. If there is a syndrome, what is its cause or causes? There are plenty of possible culprits: low doses of nerve agents (NA) that were used elsewhere by either Saddam’s regime or accidentally from an explosion of an ammunition depot; pesticides, which were widely used against mosquitoes and fleas; pyridostigmine bromide (PB pill) as a prophylactic agent against organophosphorus poisoning;

vaccines against anthrax or botulism, possibly containing the long-chain hydrocarbon squalene.

No pharmacological treatments have been demonstrated to effectively treat GWS in Gulf War veterans. Recent study of Golier et al. (2016) with the glucocorticoid receptor antagonist mifepristone was negative for the primary and secondary clinical outcomes. However, the data suggest a moderate dose of mifepristone may have circumscribed cognitive-enhancing effects in GWS.

A similar problem as a treatment of GWS is its diagnosis (Minshall, 2014). Recently, in June 28, 2016, the article of Dr. Gerhard Johnson and its coworkers, with VA and the University of Minnesota (Johnson et al., 2016), appeared in the journal PLOS ONE based on a study of 85 Gulf War veterans. Authors have developed a tentative panel of blood markers that can verify a diagnosis of Gulf War Illness with 90 percent accuracy.

The results of this current study indicate that inflammation is a component of the pathobiology of GWS. Analysis of the data resulted in a model utilizing three readily measurable biomarkers that appears to significantly augment the symptom-based case definition of GWS. These new observations are highly relevant to the diagnosis of GWS, and to therapeutic trials. The method now needs validation in larger groups of patients.

REFERENCES

1. Golier JA, Caramanica K, Michaelides AC, Makotkine I, Schmeidler J, Harvey PD, Yehuda R. A randomized, double-blind, placebo-controlled, crossover trial of mifepristone in Gulf War veterans with chronic multisymptom illness. *Psychoneuroendocrinology*. **2016**, 64, 22-30.
2. GWH. Gulf war and health; Update of Health effects of serving in the gulf war. Institute of Medicine of the National Academies, USA. Washington, DC: 2010.

3. Iversen A, Chalder T, Wessely S. Gulf War Illness: lessons from medically unexplained symptoms. *Clin Psychol Rev.* **2007**, 27, 842–854.
4. Johnson GJ, Slater BCS, Leis LA, Rector TS, Bach RR. Blood biomarkers of chronic inflammation in Gulf War Illness. *Plos ONE*, June 28, **2016**.
5. Minshall D. Gulf War Syndrome: a review of current knowledge and understanding. *J R Nav Med Serv.* **2014**, 100(3), 252-8.
6. Patocka J, Honegr J, Soukup O. Gulf war syndrome – a syndrome or not? *Toxin Reviews.* **2015**, 34(1), 43-52.



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