

Review of Study of Novel Treatment of Gulf War Illness

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Abstract

Gulf War Illness (GWI) is a serious health concern for 30% of veterans who were deployed during the first Gulf War. Symptoms include reduced physical, psychological, and neuropsychological wellness and function. Research indicates that these symptoms can be linked to environmental toxins that veterans were exposed to during their time in theater. Some data suggest that continued internal exposure may be maintaining the illness, thus a detoxification procedure could be of assistance to those experiencing GWI. Reviewed here is a novel detoxification procedure applied as a treatment for GWI and the positive outcomes associated with this procedure. Presented here is a brief logic for the detoxification method, a simple summary of the method, and the encouraging outcomes of the method. Awareness of this and similar detoxification methods' impacts on GWI symptoms should highlight the need for more research on this and related topics.

It has been estimated that up to 30% of veterans who served in the Gulf War still suffer from serious health problems associated with their exposure to environmental toxins^{1,2}. A cluster of symptoms that indicated a reduction in physical and psychological wellness and neuropsychological function was associated with serving in the 1990-1991 war and has been labeled Gulf War Illness (GWI). The Research Advisory Committee on Gulf War Veterans' Illnesses (RACGWI) noted that "evidence strongly and consistently indicates" that exposure to pesticides is causally associated with GWI³. In addition, the study mentions that low-level exposure to nerve agents, close proximity to oil well fires, receipt of multiple vaccines, and effects of combinations of exposures could not be ruled out as causes of GWI. While depleted uranium and polycyclic aromatic hydrocarbons have been assessed directly^{4,5}, other contaminants such as polychlorinated biphenyls and sulfur mustard have only been assessed indirectly^{6,7}, but both methods of assessment have indicated the possibility for exposure in the Gulf War (GW) environment. The evidence strongly indicates that wartime exposure to environmental toxins continues to play a role in veterans' ongoing experiences with GWI. The exact cause of GWI is debated and is likely a combination of factors, but neurotoxic exposures certainly seem related to nervous system dysfunction observed in these veterans. The data reported by RACGWI suggest that internal exposure be considered³. But does the persistence of GWI have to do with the body's storage of these toxins these many years later?

A meta-analysis compared service members who were deployed in the GW to those who were not deployed in the GW and found

that measures of memory, executive function, and visuomotor skills were depressed for those deployed⁸. Researchers identified an association between decrements in psychological functioning and decrements in cognitive functioning in Gulf War Veterans (GWV)⁹. In addition, researchers found that GWV's have numerous physical health concerns ranging from chronic musculoskeletal pain, headaches, fatigue, insomnia, cognitive problems, poor balance, rash, dyspnea, gastrointestinal symptoms, and sensitivity to odors^{10,11}. The Kansas case criteria for GWI includes many of the above mentioned symptoms¹².

The 2014 RACGWI-updated report assumes that GWI is associated with continued effects of toxic exposure or from residual toxins taken in during the GW and noted that a clinical trial of a detoxification approach which could either reduce the burden of the toxins or reduce the toxic effects on psychological, neuro-psychological, and physical functioning was underway¹³. Researchers have taken on this question by applying a novel detoxification program, the Hubbard detoxification method (HDM)^{14,15}, to those meeting the GWI criteria^{16,17}. The goal of the detoxification process was to reduce the body's burden of toxins and enhance endogenous systems of biotransformation and elimination.

The HDM is based upon the theory that the body has the capacity to mobilize and excrete lipophilic and other xenobiotics; and that this can be achieved with a step-by-step plan that includes exercise, sauna, and nutritional supplements. The method starts with approximately 30 minutes of light aerobic exercise followed by two to four hours of sweating in a low-temperature sauna, in addition to niacin, electrolytes, polyunsaturated oils, minerals, and vitamins ingested during the daily program. The program typically lasts between three to five weeks. The HDM has been applied to persistent lipophilic xenobiotics (PBBs, PCBs, DDE) and has been successful in reducing these toxicants^{18,19}. The detoxification method has been applied to varying toxicant exposed populations with chronic symptoms reminiscent of GWI veterans, with positive outcomes such as increases in cognitive²⁰, neurocognitive function²¹, and quality of life measures²². The work of Kerr and colleagues¹⁶ represents a significant application and test of the detoxification method.

The instrumentation of Kerr and colleagues' studies was chosen to quantify the symptoms identified by the meta-analysis⁸ in order to detect changes in cognitive functioning, such as attention, executive function, visuospatial skills, and learning/memory, as well as psychological symptoms. The researchers identified positive changes in psychological, neuropsychological, and physical symptom clusters in response to the detoxification method. Eight of nine measures of psychological symptoms (anxiety, depression, hostility, interpersonal sensitivity,

obsessive-compulsive, psychoticism, somatization, and paranoid ideation) showed improvements from before the intervention and the seven-day follow-up (while phobic anxiety remained stable and at low levels). Six measures maintained those improvements at a three-month follow-up (anxiety, depression, hostility, obsessive-compulsive, somatization, and paranoid ideation)¹⁷. Neuropsychological measures indicated that eight of ten of these measures improved from before intervention and the seven-day follow-up (logical memory 1, logical memory 2, family pictures 1, trail marking A, trail marking B, dominant hand grooved pegboard, Stroop words total, and Stroop colors total; while family pictures 2 and Stroop color-word remained stable), with sustained improvement in seven of those measures at the three-month follow-up (logical memory 1, family pictures 1, trail marking A, trail marking B, dominant hand grooved pegboard, Stroop words total, and Stroop colors total)¹⁷. Kerr and colleagues reported a clinically relevant improvement compared to controls in health-related quality of life, and levels of pain and fatigue¹⁶. The ShortForm36 (VR-36) for veterans includes 8 subscales of which 5 (role-physical, bodily pain, general health, vitality, and mental health) improved. Improvements were also seen in the McGill total pain score and all subscales of the Multidimensional fatigue inventory (MFI). Thus, for the physical symptoms measured, the findings were improvements in the majority of the measures (16 of 19) at the seven-day follow-up that were maintained at the three-month follow-up (13 of 16)¹⁶. The improvement in the VR-36 vitality sub measure was consistent with improvements seen in other HDM studies²² and the MFI improvements surpassed those found in other GWI research²³. In addition, 29% of the participants who completed the 3-month follow-up were no longer classified by the Kansas case criteria as having GWI¹⁶.

Overall, the HDM had a positive impact on the three symptoms sets of GWI that were measured, and the effects of this impact were sustained overtime. The method was shown to be safe and well-tolerated and could be a benefit to other veterans who have had toxicant exposures. These findings are indirect support for the reduction of residual toxins in the GWV's body. See Table 1 for an overview of the detoxification papers mentioned within this review for more evidence. A direct measure is needed to fully evaluate the value of the detoxification program; however, the results, as presented, show very positive implications for improved health at all levels, for those affected with the above noted illnesses.

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Table 1: Summary of Detoxification Papers Presented in this Review

Study	Sample	Outcome Measures	Key Findings	Comments
Kerr et al., 2019 ¹⁶	Randomized, controlled, pilot study of ill Gulf War veterans (n=32) with HM intervention (n=22) compared to four-week waitlist control (n=10) and 3 month follow up.	Veterans RAND SF-36) McGill pain, Multidimensional fatigue inventory Neuropsychological batteries.	Mean SF-36 physical component summary score after the intervention was 6.9 (95% CI; 0.3, 14.2) points higher compared to waitlist control and 11 of 16 quality of life, pain and fatigue measures improved.	Funded by US DOD.
Morse et al., 2019 ¹⁷	Ill Gulf War veterans (trial methods as above). Pooled between group differences for baseline (n=32) and post-intervention 7 days (n=31) and 3 months (n=21)	Grooved Pegboard Test; Wechsler Memory Scale III, Trail Making Test Parts A and B, Stroop Color and Word Test. Symptom Checklist 90-Revised	Baseline comparison revealed improvement in 16 of 19 improved test scores for measures of psychological function; somatization, obsessive compulsive, depression, anxiety, hostility, and paranoid ideation and for neuropsychological function including memory, executive skill, concentration, and hand eye coordination at 7-day follow-up and 13 of 19 remained stable at 3 months. (p<0.001)	As above
Tretjak et al., 1990 ¹⁸	Case report female capacitor worker highly exposed to PCBs	PCBs in adipose, serum, skin oils and nipple discharge.	Adipose 102 ppm reduced to 37 ppm; serum 512 ppm reduced to 261 ppm; skin lipids measured 66 ppm; nipple discharge 712 ppm - ceased during treatment.	Multisymptom illness resolved at end of treatment.
Schnare et al., 1984 ¹⁹	Healthy males (n=7) age 20-30	Adipose levels of 6 PBB congeners, 7 PCB congeners, DDE, heptachlor epoxide and dieldrin pre, post and at 4-month post treatment follow-up	Reduction total PBBs of 34% and total PCBs of 34% (p<0.05) with 58% at and 38% at follow-up (p<0.01).	Persistence in humans of PBBs well established. Lean body mass before and after showed a 0.45% reduction in body fat(n.s.), demonstrating true body burden reductions rather than compartment shift.
Schnare et al., 1982 ²⁰	Group with mixed exposures including illicit drugs (n=103) and controls (n=19).	Wechsler Adult Intelligence Scale IQ and Minnesota Multiphasic Personality Inventory	On the Wechsler Adult Intelligence Scale IQ there was a mean increase in of 6.7 points (p<0.001). On the Minnesota Multiphasic Personality Inventory profiles decreased on most scales with large reductions on scale 3 (hysteria) and 4 (amoral, asocial) (p<0.01).	
Kilburn et al., 1989 ²¹	Firemen exposed to PCBs and byproducts in a transformer fire and explosion (n=14) poorer neurocognitive test scores than non exposed matched firemen (n=14) from the same city	Neurobehavioural test battery before and after protocol: memory, cognitive and perceptual motor speed via stories, visual images, & digits backwards, block design, embedded figures, Culture Fair, trail making and choice reaction time.	Following treatment memory tests were improved. For both stories and visual reproduction, Trails B, a cognitive and motor performance test, and cognitive functions measured by block designs and embedded figures improved significantly (p<0.05), and the improvement in Culture Fair was just short of significant.	Impairment in memory and cognitive function compared to controls had been protracted and was tested 6 months after exposure in the fire.
Ross et al., 2012 ²²	Retrospective chart evaluation of symptomatic police officers exposed to methamphetamine labs (n=69) pre and post HM regimen	RAND SF-36 Singer neurotoxicity questionnaire	Mean SF-36 scores improved post-treatment, (p < 0.001) Mean neurotoxicity score (n=38) improved (p < 0.001)	Treatment funded by Utah state and US government grants.

conclusions, and recommendations are theirs alone and are not necessarily endorsed by the Department of Defense.

Conflicts of Interest

The authors declare no conflict of interest. Study design, data collection methods, statistical analyses,

interpretation of the outcomes, manuscript development, and the decision to publish the results were not influenced by the funders.

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