# A Detoxification Treatment for Gulf War Illness

Findings from a study funded by the Congressionally Directed Military Research Program

## Gulf War Illness: Three decades later, veterans are still waiting for help

Approximately 30 percent of the 700,000 US veterans of the 1990–1991 Persian Gulf War developed "Gulf War Illness" (GWI) - multiple persistent symptoms that include chronic musculoskeletal pain, headaches, fatigue, insomnia, cognitive problems, poor balance, rash, breathing difficulties, gastrointestinal symptoms and sensitivity to odors.

Hundreds of millions of dollars have been invested in research, but after 30 years the exact cause remains uncertain. Even so, there is considerable evidence that toxic exposures could be a factor in the health problems that veterans are experiencing.

A recent study funded through the Congressionally Directed Military Research Program evaluated a therapy designed to address the impact of such exposures, with promising results.

## Gulf War Illness Research Program

The Gulf War Illness Research Program (GWIRP) was created in 2006. It is a competitive program that funds peer-reviewed research investigating both the causes and potential treatments for GWI.

In 2008, the GWIRP announced the availability of funding for clinical trials, seeking "proposals that will contribute to identification of effective treatments for GWI." The announcement noted that research funded by the program might include "smaller-scale pilot trials of treatments that have not previously been studied for their effectiveness in treating GWI."

## Addressing Body Burden

One of the projects that was awarded funding under the program was a study led by David Carpenter, MD, director of the Institute for Health and Environment of the University at Albany, in partnership with scientists from Sage College and the University of Toronto.

Findings from this work have recently been published in the *International Journal of Environmental Research and Public Health.*

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# A Detoxification Intervention for Gulf War Illness: A Pilot Randomized Controlled Trial

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**Abstract:** Approximately 30% of the 700,000 US veterans of the 1990–1991 Persian Gulf War developed multiple persistent symptoms called Gulf War illness. While the etiology is uncertain, several toxic

**There is no effective medical treatment. An intervention to enhance detoxification developed by Hubbard has improved quality of life and/or reduced body burdens in other cohorts.**

**We evaluated its feasibility and efficacy in ill Gulf War (GW) veterans in a randomized, waitlist-controlled, pilot study at a community-based rehabilitation facility in the United States.**

and 11 of 16 quality of life, pain and fatigue measures improved, with no serious adverse events. Most improvements were retained after 3 months. The Hubbard regimen was feasible, safe and might offer relief for symptoms of GW illness.

**Keywords:** Gulf War illness; pesticides; organophosphates; chemical warfare agents; exposure; exposome; Hubbard; sauna; detoxification; nicotinic acid; Veteran's SF-36

## 1. Introduction

A total of 956,000 military personnel, including about 700,000 from the US, served in the 1990–1991 Persian Gulf War. Within two years following service, approximately 30% of US veterans had developed persistent health effects in a complex multi symptom but variable illness pattern referred to as Gulf War Illness (GWI). Allied countries including UK, Canada, Australia and others also reported increased illness in their Gulf War veterans [1]. Symptoms of GWI include chronic musculoskeletal pain, headaches, fatigue, insomnia, cognitive problems, poor balance, rash, dyspnea, gastrointestinal symptoms and sensitivity to odors [2,3].



The researchers noted that despite the large number of exposed veterans, and the passage of three decades, there is a need for ways to help those affected by Gulf War Veterans.

function over time have been documented in long term follow-up studies of GW veterans [60,61]. This design, allowing the waitlist participants to receive the intervention after 4–6 weeks, presented a limitation however, in that we had no untreated waitlist-control 3 month follow-up data as a comparison for the immediate start group. Another limitation was that with small sample size, even with randomization, the groups could be dissimilar; thus, we used adjustment of baseline scores using analysis of covariance (ANCOVA).

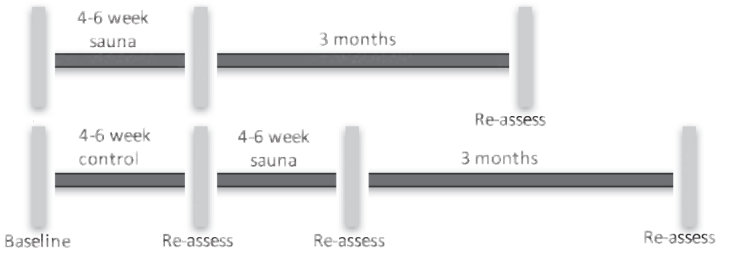


**Figure 1.** Timeline of assessment points for sauna intervention and waitlist control groups. Vertical bars indicate assessments of all outcomes were performed. Horizontal lines indicate the time frame of

**Human participants' research ethics approval was obtained from all participating institutions including Chesapeake Institutional Review Board (IRB), Columbia, Maryland (Pro00007192) after delegation to this IRB by the sponsoring institution, the University at Albany; the Sage Colleges, Troy, New York; Women's College Hospital affiliated with the University of Toronto, Toronto, Ontario, Canada; and the Human Research Protection Office (HRPO) of the Department of Defense, U.S. Army Medical Research and Development Command.**

**We obtained Food and Drug Administration Investigational New Drug approval for crystalline niacin + heat and exercise (FDA IND # 118015).**

Participants were a self-selected sample of Persian GW veterans, defined as having been deployed to the Persian Gulf between August 1990 and July 1991 and found eligible if they met the Kansas case criteria for GWI, which requires moderately severe and/or multiple symptoms in at least three of six symptom domains that first became a problem during or after the 1990–1991 Gulf War [62]. These domains include fatigue, pain, neurological/cognitive/mood, skin, gastrointestinal and respiratory. Each symptom scores 0–3 and to define a case of GWI requires a total score of 2 or greater in at least three of six symptom domains. Although there is as of yet no validated case definition for GWI, in 2014, the Institute of Medicine (IOM) recommended this case definition as best reflecting the symptom complexes of GWI [63]. Per the Kansas criteria, veterans were excluded if they had been diagnosed by a physician with serious chronic conditions, such as cancer, heart disease, liver disease, multiple sclerosis not associated with GW service but involving diverse symptoms, e.g., fatigue, cognitive problems, or pain, similar to those affecting GWI veterans, or conditions that might interfere with a veteran's ability to report symptoms, e.g., serious psychiatric conditions such as bipolar disease, schizophrenia or a history of hospitalization in the past two years for depression, alcohol, drug dependence or post-traumatic stress disorder.

The proposed research was approved by all participating universities.

### 2.5. Intervention

The regimen was administered daily seven days per week. Supervisors were in attendance throughout each session and a senior supervisor reviewed each day's reports and provided written guidance for the next day. The staff was trained according to a detailed manual covering all aspects of the Hubbard method. They were also trained in first aid and in preventing potential problems from use of a sauna or exercise equipment, e.g., heat stress, dehydration, over-hydration, fainting and injury, with special regard to any accommodations required due to symptoms of GWI. Each daily session began with a brief interview to document recent symptoms, hours slept, food eaten, any vitamins or medications taken since the previous day, weight, blood pressure and heart rate. Doses of supplements administered that day were documented on the form. At the end of the day interview, the supervisor noted down what had occurred during the program, weight, blood pressure and heart rate. In addition, the participants themselves documented minutes exercised, hours in and out of the sauna, salt or potassium supplement doses taken, new symptoms that day, realizations during the session and any questions they had.

Each session started with drinking the specific dose of powdered crystalline niacin (immediate release) dissolved in a glass of water, followed by 20–30 min on a treadmill, exercise bike or elliptical machine at a moderate aerobic level as tolerated. Often the expected niacin flush would begin during

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**The next two to four hours were spent in the low temperature (60–80 C/86-140 F), well-ventilated, Finnish sauna with cool-off breaks, showers, fluids, electrolytes and food as needed, overseen by the supervisor...**

**The other vitamin/mineral supplements were administered throughout the day with glasses of calcium-magnesium (Cal-Mag) drink.**

dose of 5000 mg for the last few days

We purchased the nutritional supplements from a single supplier, Dr. Price's Vitamins, Los Angeles (Supplement 1) whose raw materials were manufactured by Bactolac Pharmaceuticals, Hauppauge, New York, USA, a facility certified as having passed a Good Manufacturing Practices and Food Safety Systems Audit. Consistency and potency were independently verified by additional testing and documented with Certificates of Analysis for each lot. Supplements were either stored in dark cabinets or refrigerated at the facility and counted and assembled for use for each participant daily.

### 2.6. Waitlist Control

All participants allocated to the waitlist control group were required to complete baseline tests, go home and then return to the facility after 4–6 weeks to redo the assessments. They were continued during this time on treatment as usual, taking any previously prescribed medications such as for hypertension, diabetes, hypothyroidism etc. Participants from out of town were assisted with local housing during the waitlist period if the travel was too far.

Study participants underwent the Hubbard detoxification program under the supervision of a medical doctor and program administrators. The daily regimen included daily, sauna and nutritional supplements.

in a GWI trial who noted that changes of this magnitude had previously been shown to be clinically relevant in studies of chronic illnesses. However, others have estimated that an increase of 3–5 points is also clinically meaningful [72]. For the vitality subscale a 7–11 point increase was cited from a systematic review [73]. Of special interest in our study were the vitality, role-physical and social functioning subscales of the VR-36, which have been found to be sensitive and specific indicators of disability in patients with chronic fatigue syndrome [74].

2.8.4. Symptoms and Case Status

We assessed change in participants' pain symptoms with the revised short-form McGill Pain questionnaire (SF-MPQ-2) [75], which uses recall during the past week of 22 descriptors in four subscales: continuous pain, intermittent pain, neuropathic pain, affective descriptors measured from 0-10. The total pain score is the mean of the 22-item scores. The SF-MPQ-2 has been widely used, including for assessing pain in many chronic conditions and in US veterans [76], and has established reliability and validity [77], including test-retest reliability [78]. A minimally important difference would be expected at a decrease of 2 points [73,79].

We assessed changes in fatigue symptoms with the Multidimensional Fatigue Inventory (MFI), composed of five subscales: general fatigue, physical fatigue, reduced activity, mental fatigue and

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**We assessed changes in fatigue symptoms with the Multidimensional Fatigue Inventory (MFI), composed of five subscales: general fatigue, physical fatigue, reduced activity, mental fatigue and reduced motivation...The MFI has been used in other studies of GWI..**

**We used the section of the Kansas Gulf War Veterans Health Project Questionnaire, which covers 30 symptom items in six domains, both to track overall symptom burden and to assess whether the participants continued to meet the Kansas case criteria over time...**

important improvement of 7 points on the VR-36 Physical Component Summary and improvements in other health measures. Due to time and budget constraints, it was necessary one year into the study to get HRPO approval to reduce our planned sample size to 30.

We reported feasibility and safety outcomes descriptively as frequencies or percentages. We summarized the descriptive data of symptoms and quality of life outcomes with means and SDs for continuous outcomes and then constructed a model to examine the treatment effect on the VR-36 domains and other symptom measures at 7-days post treatment or waitlist (4–6 weeks time point), while controlling for baseline, using an analysis of covariance (ANCOVA). We did a complete case, intention to treat analysis. Similarly, we also performed an ANCOVA to assess any difference between the immediate sauna group and waitlisted group at 3 months, as the control group had begun their intervention 6 weeks later than the intervention group. For the control group the second baseline at the end of the 4–6 weeks waitlist was used. To assess stability of any improvements, a mixed effects model compared groups from baseline to the 3-month follow-up. Analyses were performed using R language version 3.5.1 for statistical computing (R Foundation for Statistical Computing, Vienna, Austria).

The study team evaluated the well- being of participants before and after detoxification with a variety of well-established health surveys. Quality of life was assessed with the RAND SF-36, a validated and widely-used 36 questionnaire. Symptoms were tracked using several additional tools that have been used in other Gulf War studies.

Institute of Medicine [10], the validity of this case definition is still undetermined and its natural history of variation of scores among ill Gulf War veterans has not been studied. None of the current case definitions fully account for the clinical heterogeneity commonly seen in veterans with Gulf War Illness; for instance, some veterans with GWI do not have pain, while with others pain is severe. Thus, we may be misestimating some of the improvements we are reporting regarding which particular veterans might benefit, or how much [131]. The study did not include any objective biomarkers, and was not designed to test the hypothesis that the Hubbard detoxification program results in reduction of body burden of xenobiotics. However, we have a biobank of >100 serum samples from the participants at each time point for later analysis for persistent chemicals, should funding become available.

This pilot project has generated observations that can be utilized in a future definitive trial. A future RCT would need to highlight the requirement for several weeks of time commitment for participants, which is doubled for those in a waitlist control group, to avoid misunderstandings. It would be advisable to exclude veterans with Crohn's disease or prior bowel resection due to the gastrointestinal effects of multiple supplements ingestion. Follow-ups should be made available by secure web access especially for participants who live at a distance from the facility. Follow-ups for period longer than 3 months would also be valuable.

Ideally, a future study would include biomarkers of GWI case status, such as serum autoantibodies [38], or other objective measures such as longer term follow-up changes in hippocampal

**Our study provides preliminary evidence of sustained improvement in a number of measures ofhuman health and function in GWI veterans after application of the Hubbard detoxification program. The intervention was safe and well-tolerated and the study was feasible with an acceptable recruitment rate and excellent retention through the sauna intervention.**

**The estimated benefits to the GWI veterans in our study suggest potential value to the larger veteran population who may have other deployment exposures such as burn pits, and for civilians with other toxicant exposures.**

conclusions from a recent review [3], "the identification of treatments for the GW veteran population will have far-reaching implications for treating other groups of ill patients for whom no effective treatments have been identified", and as such, it provides a measure of hope which should be expanded to a larger RCT.

**Supplementary Materials:** The following are available online at http://www.mdpi.com/1660-4601/16/21/4143/s1, Supplement 1: Investigator's Brochure, Table S1: Mean change in outcomes from pre-intervention baseline to 3 months post intervention within groups and adjusted differences between groups at 3 months, Table S2: Lab Results Dataset, Table S3: Adverse events.

**Author Contributions:** Conceptualization, D.O.C., K.K. and G.M.; methodology, D.O.C., K.K. and G.M.; formal Analysis, D.G. and F.Z.; data curation, K.K., D.O.C., G.M. and A.M., writing—original draft preparation, D.O.C., G.M. and K.K. writing—review and editing, D.O.C., K.K., G.M., F.Z., D.G. and A.L.; funding acquisition, D.O.C.

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**Acknowledgments:** We thank Maria Romero for her care and expertise as the Study Physician, Crystal Grant for her tireless work as the Study Coordinator and George Yu, George Washington University Hospital, for his guidance as independent Research Monitor. We thank the Gulf War Illness veterans who participated in this study for their motivation and dedication, the staff of the Severna Park Health and Wellness Center for their daily help. We thank retired Army Sgt. 1st Class Larry Barber for his great assistance with recruitment. We especially thank Greg Baur, Jim Avery and the many other volunteers of the Evangelical Presbyterian Church in Annapolis, Maryland, for their kind and generous help in providing housing, air fare and some meals for our Gulf War

After analyzing the data collected during the study, the researchers concluded that detoxification did show promise as an intervention for veterans affected by GWI.

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Ideally, a future study would include biomarkers of GWI case status, such as serum autoantibodies [38], or other objective measures such as longer term follow-up changes in hippocampal microstructure [132]. Additionally, biomarkers should be obtained that would represent, in real time, the enhanced detoxification process such as changes in adipose, serum or skin lipids xenobiotic

**The intervention has the potential to provide benefit with minimal disruption of the lives of individuals. This aligns with conclusions from a recent review, "the identification of treatments for the GW veteran population will have far-reaching implications for treating other groups of ill patients for whom no effective treatments have been identified", and as such, it provides a measure of hope which should be expanded to a larger RCT [randomized control group].**

exposures such as burn pits [139], and for civilians with other toxicant exposures. The intervention has the potential to provide benefit with minimal disruption of the lives of individuals. This aligns with conclusions from a recent review [3], "the identification of treatments for the GW veteran population will have far-reaching implications for treating other groups of ill patients for whom no effective treatments have been identified", and as such, it provides a measure of hope which should be expanded to a larger RCT.

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The researchers also suggested that the program could have benefits for those affected by exposures similar to those experienced by Gulf War veterans, and who have inadequate options for treatment.

## Appendices

Studies of the Hubbard Program: Reduction of Body Burden

| Study | Sample | Organohalide Tests |
|---|---|---|
| Schnare, 198491 | 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 |
| Schnare, 198692, | Healthy male electrical workers (n=10) with ongoing occupational exposure to HCB and PCBs, treated (n=5), matched controls (n=5) | Adipose, serum and skin oil levels of HCB, 5 chlorinated pesticides and 9 PCB congeners pre, post and at 3-month follow-up. Participant serum levels measured at 4 day intervals during treatment. |
| Tretjak,199093 | Symptomatic male capacitor workers (n=11) and male matched co-workers as controls (n=13) with high exposures to PCBs in Semic, Yugoslavia | Adipose and serum levels of 18 PCB congeners, before, after and at 4-month post treatment follow-up. Adipose levels ranged from 22-562 ppb in serum and 2-77 ppm in fat. |
| Tretjak, 199082 | Case report female capacitor worker highly exposed to PCBs | PCBs in adipose, serum, skin oils and nipple discharge. |
| Dahlgren, 200794 | Personnel (n=7) exposed due to the collapse and subsequent fire of the World Trade Center (WTC) September 11, 2001. | Serum PCBs and dioxins |

| Key Findings | Comments |
| --- | --- |
| 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. |
| Adjusted for re-exposure as represented in the control group, HCB body burdens were reduced by 30% post and 28% at 3 months. Mean reduction of PCBs was 16% post and 14% at 3 months. Analysis of variance indicates these reductions are statistically significant (f less than 0.001). Enhanced excretion appeared to keep pace with mobilization, as blood-serum levels in the treatment group did not increase during treatment. | Lack of increase in serum levels during treatment suggests mobilization keeping pace with excretion. |
| For 6 treatment group A adipose PCBs decreased 30% (n.s.) and serum PCBs 42% ($p<.05$). Improvement in chloracne, rashes, dry thickened skin, conjunctivitis and eyelid swelling. | Treatment group composed of 2 sub-groups, one (B) of which had concomitant disease which had less adipose reduction. Exposure levels were high and all participants had long term symptoms of poor health. |
| 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. |
| 23.4% mean reduction by weight (lipid based) of all halocarbons. WHO-TEQ for mono-ortho PCBs was decreased by 24.4%. | |

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Compiled by the non-profit Foundation for Advancements in Science and Education (FASE). Since 1984, FASE has assisted scientists and caregivers who have implemented and evaluated the Hubbard detoxification program in sharing the results of their work.

More at www.fasenet.org
Email: info@fasenet.org

View the paper online:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6862571/