CORTEX XXX (2015) 1–26

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Special issue: Review

Recent research on Gulf War illness and other health problems in veterans of the 1991 Gulf War: Effects of toxicant exposures during deployment

Roberta F. White [a,*], Lea Steele [b], James P. O'Callaghan [c], Kimberly Sullivan [d], James H. Binns [e], Beatrice A. Golomb [f], Floyd E. Bloom [g], James A. Bunker [h], Fiona Crawford [i], Joel C. Graves [j], Anthony Hardie [k], Nancy Klimas [l], Marguerite Knox [m], William J. Meggs [n], Jack Melling [o], Martin A. Philbert [p] and Rachel Grashow [q]

[a] Department of Environmental Health, Environmental Health, Boston University School of Public Health, Boston, MA, United States
[b] Baylor University Institute of Biomedical Studies, Waco, TX, United States
[c] Molecular Neurotoxicology, Toxicology & Molecular Biology Branch (MS-3014), Health Effects Laboratory Division, Centers for Disease Control and Prevention – NIOSH, Morgantown, WV, United States
[d] Boston University School of Public Health, Department of Environmental Health, Boston, MA, United States
[e] Research Advisory Committee on Gulf War Veterans' Illnesses, Phoenix, AZ, United States
[f] University of California, San Diego, La Jolla, CA, United States
[g] Molecular & Integrative Neuroscience Department, The Scripps Research Institute, La Jolla, CA, United States
[h] National Gulf War Resource Center, Topeka, KS, United States
[i] Roskamp Institute, Sarasota, FL, United States
[j] Crestview, FL, United States
[k] Bradenton, FL, United States
[l] Nova Southeastern University Algy/Imm, Miami, FL, United States
[m] McEntire Joint National Guard Base, Eastover, SC, United States
[n] Department of Emergency Medicine, 3ED311, The Brody School of Medicine, East Carolina University School of Medicine, Greenville, NC, United States
[o] U.S. Government Accountability Office, Salisbury, Wiltshire, UK
[p] School of Public Health, Ann Arbor, MI, United States
[q] Northeastern University, Department of Environmental and Civil Engineering, Boston, MA, United States

* Corresponding author. Department of Environmental Health, Environmental Health, Boston University School of Public Health, 715 Albany St., T4W, Boston, MA 02118, United States.
E-mail addresses: rwhite@bu.edu (R.F. White), Lea_Steele@baylor.edu (L. Steele), jdo5@cdc.gov (J.P. O'Callaghan), tty@bu.edu (K. Sullivan), Binns.Jim@gmail.com (J.H. Binns), bgolomb@popmail.ucsd.edu (B.A. Golomb), fbloom@bloomsciassocs.net, fbloom@scripps.edu (F.E. Bloom), desert-storm1991@outlook.com (J.A. Bunker), fcrawford@RFDN.ORG (F. Crawford), joelcgraves@gmail.com (J.C. Graves), anthony.d.hardie@gmail.com (A. Hardie), nklimas@nova.edu (N. Klimas), marguerite.knox@us.army.mil, marguerite.l.knox.mil@mail.mil (M. Knox), meggsw@ecu.edu (W.J. Meggs), jmelling@ptd.net (J. Melling), Philbert@umich.edu (M.A. Philbert), r.grashow@neu.edu (R. Grashow).
http://dx.doi.org/10.1016/j.cortex.2015.08.022

Please cite this article in press as: White, R. F., et al., Recent research on Gulf War illness and other health problems in veterans of the 1991 Gulf War: Effects of toxicant exposures during deployment, Cortex (2015), http://dx.doi.org/10.1016/j.cortex.2015.08.022

ARTICLE INFO

Article history:
Received 20 March 2015
Reviewed 18 June 2015
Revised 19 August 2015
Accepted 28 August 2015
Published online xxx

Keywords:
Gulf War illness
Pesticide
Organophosphates
Sarin
Cyclosarin
Veterans' health

ABSTRACT

Veterans of the 1991 Gulf War (GW) are a unique population of veterans who returned from theater with multiple health complaints and disorders. Studies in the U.S. and elsewhere have consistently concluded that approximately 25–32% of this population suffers from a disorder characterized by symptoms that vary somewhat among individuals and include fatigue, headaches, cognitive dysfunction, musculoskeletal pain, and respiratory, gastrointestinal and dermatologic complaints. Gulf War illness (GWI) is the term used to describe this disorder. In addition, brain cancer occurs at increased rates in subgroups of GW veterans, as do neuropsychological and brain imaging abnormalities.

Chemical exposures have become the focus of etiologic GWI research because nervous system symptoms are prominent and many neurotoxicants were present in theater, including organophosphates (OPs), carbamates, and other pesticides; sarin/cyclosarin nerve agents, and pyridostigmine bromide (PB) medications used as prophylaxis against chemical warfare attacks. Psychiatric etiologies have been ruled out.

This paper reviews the recent literature on the health of 1991 GW veterans, focusing particularly on the central nervous system and on effects of toxicant exposures. In addition, it emphasizes research published since 2008, following on an exhaustive review that was published in that year that summarizes the prior literature (RACGWI, 2008).

We conclude that exposure to pesticides and/or to PB are causally associated with GWI and the neurological dysfunction in GW veterans. Exposure to sarin and cyclosarin and to oil well fire emissions are also associated with neurologically based health effects, though their contribution to development of the disorder known as GWI is less clear. Gene-environment interactions are likely to have contributed to development of GWI in deployed veterans. The health consequences of chemical exposures in the GW and other conflicts have been called "toxic wounds" by veterans. This type of injury requires further study and concentrated treatment research efforts that may also benefit other occupational groups with similar exposure-related illnesses.

1. Introduction

The 1991 Gulf War (GW) was fought by a multinational coalition that formed to oppose Iraq's invasion of Kuwait in 1990. The coalition included nearly 700,000 U.S. troops as well as soldiers from the United Kingdom, Canada, Australia, and France, with over 30 partnering countries. It began with a build-up of troops in the region (Operation Desert Shield) prior to the actual conflict (Operation Desert Storm), which included a six-week air campaign and four days of ground fighting before a ceasefire was declared on February 28, 1991. This was followed by the return of the majority of the troops by the spring of 1991. There were few casualties on the winning side. The GW was remarkable for the numbers of chemical exposures experienced by troops, including the low-level chemical warfare agents released by the destruction of Iraqi facilities, extensive spraying and use of pesticides, and hundreds of oil well fires set by the Iraqi troops as they withdrew from Kuwait.

Within a year of return from the GW, it became apparent that troops were suffering from a variety of symptoms that were difficult to explain by health care providers, who did not recognize a typical medical illness in the veterans. Initially dubbed "GW syndrome" by the press, this disorder appeared to affect many, but not all, GW veterans. Fatigue, widespread pain, cognitive and memory problems, skin rashes, gastrointestinal and respiratory difficulties were commonly reported, but not every veteran afflicted by GW illness (GWI) presented with identical symptoms. Intensive research was initiated to characterize the disorder, understand its prevalence, investigate likely causes, and explore possible mechanisms of disease. Although the troops and some health care providers immediately suspected that chemical exposures were the cause of the condition, others ascribed GWI to post-traumatic stress disorder (PTSD) or other psychiatric conditions, or to the usual consequence of all wars. Effective treatments for GWI have been elusive but recently a treatment research effort has begun to flourish.

This paper explores the characteristics of GWI, its definition and prevalence (Epidemiology of GWI), the conditions in theater that may have caused GWI and specific indictors of nervous system dysfunction (Persistent Health Effects in GW Veterans in Relation to Deployment Experiences and Exposures), physiological mechanisms underlying GWI (Pathobiology) and experimental models of GWI and its causation (Animal Studies). It also summarizes current evidence related to a variety of neurological outcomes in addition to GWI that have been significantly associated with self-reported or modeled chemical exposures encountered by veterans during the GW. The paper is based on a recent summary of GWI research, *Gulf War illness and the health of Gulf War veterans:*

Please cite this article in press as: White, R. F., et al., Recent research on Gulf War illness and other health problems in veterans of the 1991 Gulf War: Effects of toxicant exposures during deployment, Cortex (2015), http://dx.doi.org/10.1016/j.cortex.2015.08.022