

A majority of the American military personnel who served during Operations Desert Shield and Desert Storm (ODS/DS)¹ were exposed to personal or field-use pesticides. Although toxicity may vary by individual, it is known that pesticides, when used improperly, can result in health problems that are similar to those experienced by some Persian Gulf War veterans (PGWV). This report examines the scientific literature pertaining to the health effects of pesticides available during ODS/DS as part of the ongoing effort to understand better the possible causes of undiagnosed symptoms among some PGWV.

The report is intended to be used in combination with two other studies undertaken to improve the understanding of pesticide exposures during ODS/DS. *Pesticide Use During the Gulf War: A Survey of Gulf War Veterans* (Fricker et al., 2000) reviews the findings of a survey of some 2,000 PGWV that attempts to quantify the use of pesticides during ODS/DS. *Pesticides Environmental Exposure Report*, being prepared by the Office of the Special Assistant for Gulf War Illnesses (OSAGWI), investigates the use of pesticides in the Gulf and the possible risk to troops who served there.

The present report reviews the scientific literature on 12 of the 35 pesticide active ingredients that were potentially used during ODS/DS.² OSAGWI asked RAND to focus on the potential health effects of these 12 compounds, which it considers to be of particular concern because of either toxicity or expected exposure. The compounds consist of five organophosphate (OP) pesticides

¹While the terms *ODS/DS*, *Persian Gulf War (PGW)*, and *Gulf War* have been used interchangeably by some authors, including those of other volumes in this series, officials in the Office of the Special Assistant for Gulf War Illnesses consider that all personnel who served in the Kuwait Theater of Operations from August 1990 to July 1991 are veterans of ODS/DS. In this report, *ODS/DS* is usually used to refer to that theater of operations; however, *PGW* and *Gulf War* are also used, reflecting the literature reviewed. Similarly, the terms *Persian Gulf War veterans (PGWV)* and *Gulf War veterans* have become synonymous with *ODS/DS veterans* in much of the literature, and both will be found in this report.

²The review was originally intended to address 11 pesticides. Bendiocarb was added after completion of the first draft.

(azamethiphos, chlorpyrifos, diazinon, dichlorvos, and malathion), three carbamate pesticides (bendiocarb, methomyl, and propoxur), two pyrethroid pesticides (permethrin and *d*-phenothrin), one organochlorine pesticide (lindane), and one repellent (DEET). The report summarizes the relevant literature and then examines the possible links between known pesticide exposures or doses and related health outcomes.

BACKGROUND

Iraq invaded Kuwait on August 2, 1990. In support of United Nations Resolution 660, the United States responded by sending troops to the Persian Gulf in Operation Desert Shield. On January 16, 1991, Operation Desert Storm commenced with an air war against Iraq that was followed, 39 days later, by a four-day ground war. The Department of Defense (DoD) has estimated that nearly 700,000 American troops served in ODS/DS.

Many PGWV have reported an array of health problems.³ The most commonly reported symptoms include joint pains, sleep disorder, memory loss, and fatigue. Studies show that these symptoms occur more frequently among PGWV than among persons who were not deployed to ODS/DS (Joseph, 1997). A variety of studies have characterized symptoms and diagnoses in PGWV, and their reported health problems are a source of continuing concern to veterans and policymakers. This concern has prompted efforts, including the present one, to evaluate whether exposures of these veterans to various risk factors during ODS/DS might be linked to their reported symptoms.

A review of military history reveals that disease and non-battle injury (DNBI) account for substantially more casualties than do battle wounds. DNBI prevalence and estimates of DNBI for future conflicts have decreased markedly in recent decades, largely due to the success of military preventive medicine practices. These essential practices include the use of pesticides to control pests that can carry and transmit diseases such as malaria or leishmaniasis. While the DNBI rate during ODS/DS was extremely low, the illnesses reported by veterans of that conflict and the absence of readily identifiable causes have led policymakers and health specialists to consider the very pesticides that ostensibly contributed to the preventive medicine success of ODS/DS as a cause of some illnesses.

METHODS

We conducted a systematic literature review in consultation with an experienced RAND librarian. This review included a detailed search of the following

³See Chapter Three.

databases: BIOSIS, CARL UnCover, CAsEarch, Chemical Abstracts, Chemtox, Embase, Medline, Scisearch, SilverPlatter Applied Science and Technology Index, and Toxline. The search terms included each of the pesticide classes (e.g., OP, carbamate) and each of the pesticides of concern (by name, synonyms, and Chemical Abstracts Service (CAS) registry number). The search also included various databases and data sources, such as those made available by the U.S. Environmental Protection Agency (EPA), state environmental agencies, and other organizations detailed in Chapter Two.

The initial search was restricted to English language articles or those with English language abstracts published between 1980 and 1998, inclusive. These dates were chosen because a search that did not restrict dates yielded more results than could be managed. The initial search resulted in over 7,000 titles. As the literature review progressed, references to articles published before 1980 were noted and such articles were retrieved as needed; articles published after 1998 were included as they became available. Articles and reports that appeared relevant based on titles resulting from this initial search were identified and accessed.

ORGANIZATION OF THE REPORT

Chapter Two provides general information about pesticides, including the history of and reasons for pesticide use, the taxonomy of pesticides, and the ways in which pesticide use is regulated in the United States. It also includes a brief discussion of the challenges of determining risk associated with pesticide use and the role this report may play in such a determination. What is currently known about pesticide availability and possible use during ODS/DS is also discussed in Chapter Two; however, the chapter does not report on specific pesticide exposures that were encountered during ODS/DS. Chapter Three discusses symptoms reported to be experienced by some ODS/DS veterans.

Chapters Four through Seven are organized by pesticide chemical class. Each deals with a specific class of pesticide and includes general information about the class, with subsections arranged by specific pesticides of concern. Each subsection includes information about the use and chemistry of a particular pesticide. Explanations of the types of information presented, including occupational health values, are included in Chapter Two. In addition, some pesticide subsections include unique information of specific interest to the study of Gulf War illnesses.

Following the specific pesticide subsections in each chapter is a review of the scientific literature related to the potential health effects of each class of pesticide. Chapters Four through Seven are generally organized in sections that present acute effects, chronic effects, genetic effects, reproductive effects, and carcinogenic effects. Exposures of animals or humans to chemicals are typically

classified into one of four categories: acute, subacute, subchronic, and chronic (Eaton and Klaasen, 1996, p. 15). Acute exposure is exposure to a chemical for less than 24 hours; usually, but not always, it refers to a single administration. Subacute exposure refers to repeated exposure for up to one month, subchronic for one to three months, and chronic for more than three months. Because not all authors use this classification scheme, we avoid strict divisions of the literature by including subacute and subchronic exposures in sections covering acute and chronic exposures, respectively. While *immediate* and *long-term* may be more appropriate as descriptors of effects, we use *acute* and *chronic* because this substitution is more prevalent in the reviewed literature. In this review, the above classifications are used where possible, but differing interpretations are recognized and stated.

The potential health effects of OP and carbamate pesticides are reviewed in a single chapter because of the toxicological similarities of these pesticide classes, as is further explained in the text. While the reviews of the potential health effects of each chemical are organized in a similar manner, there are also differences that reflect the nature of the literature.

Chapter Eight deals with confounding factors, such as interactions and individual differences, and Chapter Nine presents concluding remarks and suggests additional research.