

# ***GULF WAR RISK FACTOR REPORT REPRINTS***

## **Chemical and Biological Warfare Agents**

*The following articles originally appeared in the October 2000 issue of the Gulf War Review newsletter. For information about the newsletter, contact Mr. Donald J. Rosenblum, Deputy Director, Environmental Agents Service (131), VA Central Office, 810 Vermont Avenue, NW, Washington, DC 20420, telephone: 202-273-8580.*

## **Chemical and Biological Warfare Agents and Your Health – Researchers Search for Answers**

Chemical and biological warfare agents are materials deliberately designed to cause lethal and debilitating toxic effects or acute infectious disease in humans. In the last decades and before the Gulf War the most common warfare agents of concern were organophosphorus (OP) agents such as sarin, soman and/or VX, and blistering agents such as mustard agent.

Aerosolized (airborne) active spores of the naturally occurring bacteria anthrax (*Bacillus anthracis*) and botulinum toxin, a protein agent formed by another bacterium *Clostridium botulinum*, were the biological warfare agents of greatest concern to military planners before the Gulf War. Anthrax infections occur naturally in farm animals but are also sometimes reported in humans. Humans become infected through contact with infected animals or by inhalation of spores from infected animal products, such as hides. Poisoning by botulinum toxin is also reported in humans, often through accidental consumption of contaminated food.

## **Possible Exposure in the Gulf War**

Before the Gulf War, it was known that Iraq possessed both chemical and biological weapons, but DoD and the British Ministry of Defense have reported that Iraqi forces against coalition forces intentionally used neither chemical nor biological weapons during the Gulf War. The DoD has reported that one U.S. soldier may have received a burn in his arm from mustard agent, caused by accidental exposure while exploring a captured bunker in southern Iraq.

Just after the cease-fire was declared in Iraq, some Gulf War veterans may have been exposed to low or trace levels of chemical warfare agents. In March 1991, after the end of the Gulf War, U.S. service members used explosives to destroy a large ammunition depot at Khamisiyah in southern Iraq. It was later discovered that this site contained the nerve agents sarin and cyclosarin. During the demolition some of these agents were released into the atmosphere. Based upon the research carried out by the CIA, in 1997 DoD notified nearly 100,000 Gulf War veterans who had been in the vicinity of Khamisiyah at the time of the demolition that they could have been exposed to low-levels of these chemical agents.

The DoD has stated that no cases of acute (that is, obvious poisoning effects that occur within minutes after exposure) poisoning symptoms, which would have resulted from high-level exposure to nerve agents, were reported during the Gulf War. Nevertheless, some U.S. service members may have experienced low-level exposures from inhalation of airborne nerve agents in the Gulf War region following the 1991 cease-fire.

### **How it Enters and Leaves the Body**

Chemical warfare agents can be absorbed either by breathing vapors or by skin contact. The primary exposure concern for sarin and cyclosarin is by breathing vapors. Mustard agent is primarily absorbed by skin contact, although breathing it is also an important form of exposure. All of these chemical agents are rapidly broken down in the body and excreted, primarily in urine, following absorption by breathing or skin contact.

Infections of anthrax can occur through breathing and skin and stomach exposure. Naturally occurring anthrax infection is usually through skin contact, and most commonly occurs in farm animals. Exposure for anthrax used in weapons is through breathing aerosolized spores. Breathing in anthrax leads to pulmonary (in the lung) anthrax infection, which in non-military situations is a rare form of the disease compared to the infections of the skin and stomach.

### **What We Know and Don't Know about the Health Effects**

The OP chemical warfare agents, including sarin, cause symptoms that are virtually identical to those caused by poisoning from OP pesticides. In people who have survived severe poisoning by these compounds, studies have shown subtle but detectable neurological deficits that may last months or even years. These effects have not been described in people who have only had mild or no immediate poisoning symptoms. Research is underway to explore what might happen in people showing either very mild or even no immediate poisoning effects.

Exposure to mustard agent can cause severe irritation and tissue damage including typical blistering, to eyes, skin and respiratory and digestive tracts. The symptoms and signs of mustard agent exposure are delayed for some hours following skin contact or breathing the vapors. The mustard agents are also considered to be likely carcinogens and humans exposed to mustard agent are thought to be at some increased risk of respiratory and skin cancers in decades following exposure.

Peter Spencer, Ph.D., Oregon Health Sciences University, suggests that veterans who volunteered in the 1960's for a U.S. study of the immediate effects of chemical agents and their antidotes be screened for any evidence of delayed health effects. In fact, VA and DoD are currently sponsoring such studies.

Anthrax spores following breathing germinate up to 60 days later. After germination, illness occurs rapidly as replicating bacteria release toxins that can lead to

blood loss, swelling, and tissue damage. If left untreated, pulmonary anthrax infection is almost always fatal. There is no long-term health effects reported in individuals surviving pulmonary anthrax infection.

Symptoms caused by botulinum infection include respiratory distress and paralysis, and death can occur by suffocation. Some individuals surviving botulism poisoning from contaminated food or other natural sources experience residual weakness for as long as a year after disease onset.

### **Possible Effects with Children of Gulf War Veterans**

OP nerve agents, including pesticides and chemical warfare agents, are not considered to cause birth defects. Although a developing fetus could be affected if the mother were exposed to these agents, in general, this would not be relevant to Gulf War veterans. Mustard agents are considered to be likely human carcinogens, but current information is not sufficient to conclude that they have human reproductive health effects, especially following exposure to males.

Pulmonary anthrax is nearly always fatal if not treated immediately with antibiotics, but there is no evidence that individuals surviving anthrax infection are at increased risk for adverse reproductive health effects.

Botulinum toxin (in a purified form and in low doses) is actually licensed by the FDA for therapeutic uses as Botox®. Botulinum toxin is not considered to cause birth defects.

### **Testing to Determine Exposure?**

Nerve and blister agents are rapidly broken down in the body and excreted as metabolites indicating exposure can be detected in urine in hours or at most a few days following exposure. But metabolism and excretion of these compounds will be complete within days in cases where the individual survives the initial exposure. There is no available test today that can confirm exposure to these chemical warfare agents that may have occurred several months or years in the past. There is no generally available test to detect exposure to anthrax at levels that did not cause actual clinical manifestations of infection. The body may react to low amounts of botulinum, but there is also no conventional test for exposure that may have occurred months or years in the past.

### **What Independent Scientific Review Groups Have Concluded**

In their 1996 report, the Presidential Advisory Committee on Gulf War Illnesses (PAC) concluded that “[b]ased on available data, it is unlikely that health effects reported by Gulf War veterans today are the result of exposure to OP or mustard CW agents during the Gulf War.” Relative to biological warfare agents, the PAC concluded that “it is unlikely the health effects reported today by Gulf War veterans are the result of exposures to BW agents.” The PAC cautioned, however, that the amount of scientific

information available regarding the health effects of chemical warfare agents is not very large.

The Defense Science Board Task Force on Persian Gulf War Health Effects (DSB) concluded in their 1994 report that "...there is no indication from research that there would be chronic effects from low level exposure even if it had occurred." Relative to biological agents, the DSB concluded, "The diseases associated with BW agent, e.g., anthrax, botulinum, etc., are notable for acute effects and would have been rapidly evident and readily diagnosed had they occurred among U.S. or coalition troops during the war."

The Institute of Medicine 1996 report "Health Consequences of Service During the Persian Gulf War" (IOM) concluded that "...there is no available evidence in human or animal studies to date that exposure to nerve agents at low levels that do not produce any detectable acute clinical or physiological manifestations results in any chronic or long term adverse health effects."

In the September 2000 report described in the article above, the IOM concluded that 1) there is sufficient evidence of a causal relationship between exposure to sarin and a dose-dependent acute cholinergic-syndrome that is evident seconds to hours subsequent to sarin exposure and resolves in days and months; 2) there is limited/suggestive evidence of an association between exposure to sarin at doses sufficient to cause acute cholinergic signs and symptoms and subsequent long-term health effects; and 3) there is inadequate/insufficient evidence to determine whether an association does or does not exist between exposure to sarin at low doses insufficient to cause acute cholinergic signs and symptoms and subsequent long-term adverse health effects.

That recent IOM report also recommended additional research to augment our understanding of the long-term health effects of exposure to sarin. Specifically, the IOM recommended: 1) careful long-term follow-up of populations exposed to sarin in the Matsumoto and Tokyo terrorist attacks; 2) studies in experimental animals to investigate the long-term effects of acute, short-term sarin exposure at doses that do not cause overt cholinergic effects and cause only minimal acetylcholinesterase inhibition; and 3) research on genetic factors that may alter susceptibility to sarin toxicity.

It is important to note that all of these independent review groups caution that we do not have a great deal of information to base conclusions about long-term effects of exposure to low-levels of chemical warfare agents, and that further research is justified.

For this article, we contacted several scientists from the Department of Defense with recognized expertise with regard to the long-term health consequences of exposure to chemical and biological warfare agents. Unfortunately, because of the controversial nature of this subject we were unable to get as many comments as we would have liked. Here is some of what we were told:

Dr. Peter Spencer (identified above) commented the results of this research are relevant not only to the future health of veterans, but also to the health of Americans who live close to U.S. sites where sarin and mustard will be destroyed via incineration under an international agreement to destroy stockpiled chemical weapons.

Dr. Mark A. Brown, Director, VA's Environmental Agents Service, said that in essentially all independent reviews by scientific committees, chemical and biological warfare agents have not surfaced as the "smoking gun" cause of Gulf War illnesses.

### **What a Concerned Gulf War Veteran Should Do**

Gulf War veterans with health concerns are encouraged to contact the nearest VA medical center for a Gulf War Registry health examination. The telephone number of the medical center can be found in local telephone directories under the Department of Veterans Affairs in the "U.S. Government" listings.

Veterans with service-related disabilities may wish to file a claim for disability compensation. A veterans services representative (VSR) at the nearest VA regional office or medical center can provide the application and any needed assistance. The national toll-free telephone number to reach a VSR is 1-800-827-1000. Veterans service organizations also may be helpful to Gulf War veterans seeking benefits from VA.

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## **Federally Funded Research in Low-Level Exposures to Chemical Warfare Agents**

The federal research portfolio on Gulf War veterans' illnesses consists of some 190 funded research projects with a total budget of more than \$150 million dollars. These projects, which began in 1993, consist of fourteen major research focus areas, each devoted to determining the causes, diagnoses, and treatments for Gulf War Illnesses. A major research area that is of particular importance to Gulf War veterans is that of chemical warfare, and specifically the health effects of exposure to low-level chemical agents.

Low-level exposure to chemical agents is being studied as a possible cause of the ill health effects that some troops reportedly experienced after returning from the Gulf War. These potential encounters have prompted federally funded toxicology studies to be done examining the potential for long term adverse health effects stemming from short-term or low-level chemical exposures.

During the Gulf War, chemical detector alarms went off many times, and soldiers often had to put on their masks and protective uniforms. Some soldiers went home after the war with concerns about possible chemical agent exposures. In 1996, the Department of Defense (DoD) announced that U.S. troops might have had very low-level exposures due to the demolitions at Khamisiyah, Iraq in March 1991. Fortunately, no troops developed any symptoms of sarin exposure at the time of the demolitions.

Since early 1997, DoD's Office of the Special Assistant for Gulf War Illnesses has investigated about 20 reported incidents of possible chemical agent exposure, and published reports on each incident. In one incident, one soldier was likely to have been exposed to mustard agent while exploring an Iraqi ammunition bunker. With the exception of Khamisiyah, the conclusions for all of the other published incidents, so far, were that exposure to chemical agents were unlikely or definitely did not occur.

### **20 Projects; \$16.6 Million**

The federally-funded research on low-level chemical agents is comprised of a group of twenty projects with an overall funding of \$16.6 million dollars. Each of these twenty projects approaches from different angles the many questions regarding exposure to low dose chemical weapons. Some consider the short-term effects of specific chemical agents such as sarin or mustard agent, while others look at the long-term general health of potentially exposed veterans. Several studies are evaluating the health effects of low-level sarin exposure, in combination with pyridostigmine bromide or pesticides.

Of the twenty projects relating to the effects of chemical warfare, ten have already been completed, and another five are scheduled for completion by the end of this year. New projects are continuously being added to those already underway as the research warrants.

Although no final conclusions have been made regarding low-level exposure to chemical agents, preliminary results have shown no difference between the health outcomes of troops in exposure areas versus troops in non-exposure areas.

One major study focused on the Khamisiyah demolitions, which occurred during March of 1991 and were thought at the time to have exposed up to 100,000 veterans to subclinical levels of sarin and cyclosarin. This study did not show any long-term adverse health effects in veterans. Two other major studies of veterans with potential exposure due to the Khamisiyah demolitions will be completed next year.

The Department of Veterans Affairs, along with the Departments of Defense and of Health and Human Services, remain committed to research on potential exposures of chemical agents on Gulf War veterans. Some studies will go on for several years to come, while others will start as new information and/or new research approaches are identified.

The "Gulf War Review" will continue to provide information about these important research efforts.

