GULF WAR RISK FACTOR REPORT REPRINTS

Vaccinations, Including Anthrax and Botulinum

The following article originally appeared in the May 2001 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.*

Researchers Search for Answers About Possible Adverse Effects of Vaccinations, Including Anthrax and Botulinum

The following is part of a series of articles about various environmental hazards or risks encountered by military personnel deployed to the Gulf War theater of operations. Previous articles have focused on chemical and biological warfare agents, pesticides, depleted uranium, pyridostigmine bromide, and infectious diseases. They can be found on-line at www.va.gov/health/environ/persgulf.htm.

Before deployment in the Gulf War, all U.S. troops were given a standard series of inoculations against infectious diseases that would be provided to any U.S. citizen traveling to that part of the world. After their arrival in the theater of operations, some Gulf War participants received an additional two nonlive vaccines for protection against two biological warfare agents, anthrax and botulinum toxoid. The Department of Defense (DoD) estimates that about 8,000 troops received the botulinum vaccine, but the Food and Drug Administration (FDA)-approved anthrax was administered to a much larger group of about 150,000.

Concerns have been expressed about the possible long-term health consequences of these vaccines alone or in combination with other agents, including other vaccines. A number of studies have been approved to examine this hypothesis.

The following material regarding vaccinations received by Gulf War troops were extracted from the National Academy of Sciences' Institute of Medicine (IOM) report, entitled *Gulf War and Health: Volume 1. Depleted Uranium, Sarin, Pyridostigmine Bromide, Vaccines* (available on-line at www.nap.edu). The report, released in September 2000, focuses on the four areas of health concerns included in the subtitle. Other agents will be evaluated in future volumes.

The IOM report was required by two laws: the Veterans Programs Enhancement Act of 1998 (Public Law 105-368 and the Persian Gulf War Veterans Act of 1998 (Public Law 105-277). In reality, VA contracted with the IOM for the review several months prior to the enactment of this legislation.

The National Academy of Sciences (NAS) is a private, nongovernmental, nonprofit, independent society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of charter granted to it by Congress in 1963, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. In 1970, the NAS established the IOM to secure the services of prestigious scientists and physicians to examine important public health problems.

Concerns about Iraq's offensive biological warfare capabilities during the Gulf War led to the decision that available vaccines should be used to protect U.S. service members against biological warfare agents. DoD sent approximately 310,000 doses of FDA-licensed anthrax vaccine to the Gulf War theater of operations, and it is estimated that 150,000 U.S. troops received at least one anthrax vaccination. About 137,850 doses of botulinum toxoid were sent to the Gulf, and it is estimated that 8,000 individuals were vaccinated. However, medical records from the Gulf War contain little or no information about who received these vaccines, how frequently the vaccines were administered, or the timing of vaccinations relative to other exposures.

Anthrax Vaccine

The anthrax vaccine has long been used in humans for the protection of workers, such as persons working with animal hair or hide, including goat hair mill workers, tannery workers, and veterinarians. A license for the anthrax vaccine was granted on November 10, 1970. It is estimated that 68,000 doses of the U.S. anthrax vaccine for use in protecting U.S. civilian workers were distributed from 1974 to 1989; 268,000 doses in 1990; and 1.2 million doses from 1991 to July 1999. The exact number of people who received the vaccine is not known.

In December 1997, the Secretary of Defense announced that all U.S. military forces would receive anthrax vaccinations for protection against the threat of biological warfare. The Anthrax Vaccine Immunization Program (AVIP) began vaccinations in March 1998.

Health Effects of the Anthrax Vaccine

According to the IOM, there is little information in published peer-reviewed scientific and medical literature on the safety of the anthrax vaccine. There is some information about the immediate effects of this vaccine; however, studies of the anthrax vaccine have not actively evaluated long-term health effects. Unfortunately, this situation is typical for virtually all vaccines.

The IOM committee concluded that there is sufficient evidence of an association between anthrax vaccination and transient acute (immediate) common health effects such as redness, swelling, fever, as is typically associated with many vaccinations. The committee also found that there is inadequate/insufficient evidence to determine whether an association does or does not exist between anthrax vaccination and long-term health problems.

Botulinum Toxoid

Botulinum toxins, known primarily for causing cases of foodborne botulism poisoning, are produced by the bacterium *Clostridium botulinum*. Different strains of these bacteria produce seven distinct botulinum toxins. These toxins are among the most toxic compounds known per body weight in mice.

Work on modifying the botulinum toxin to the nontoxic form of a toxoid began in 1924. The current botulinum toxoid vaccine is in FDA's Investigational New Drug (IND) status. The toxoid has been given to volunteers for testing purposes and to occupationally at-risk workers. Recent advances in molecular cloning techniques and new knowledge about the molecular mechanisms of action of the toxins have opened up avenues for new botulinum vaccine development for the future.

Health Effects of Botulinum Toxoid

Early studies of the initial botulinum toxoids in the 1940s reported a significant number of reactions. Several studies of the botulinum toxoid vaccine also noted moderate local or systemic reactions. Studies of the botulinum toxoid vaccine have not actively looked on health problems (instead waiting for any report to come in) to evaluate long-term health problems. This situation is unfortunately typical for all but a few vaccines.

The IOM committee concluded that there is sufficient evidence of an association between botulinum toxoid vaccination and transient acute local and systemic effects (for example, redness, swelling, fever), as is typically associated with vaccination. The committee also found that there is inadequate/insufficient evidence to determine whether an association does or does not exist between botulinum toxoid vaccination and long-term adverse health effects.

Multiple Vaccinations

Military personnel often receive several vaccinations as they prepare for service in an environment with many endemic diseases. Some vaccinations are given routinely to all military recruits; others are administered for deployment to specific geographic or high-risk areas; and still others are specific to the occupational setting. Some are concerned that multiple vaccinations prior to and during Gulf War service may have caused health problems.

Health Effects of Multiple Vaccinations

Certain multiple vaccinations can lead to negative effects, but there is little evidence, largely because of a lack of active monitoring, of adverse effects beyond the transient local and systemic effects seen often with any vaccination.

A group of 99 employees at Fort Detrick, Maryland, who received many vaccinations for their jobs, were followed for up to 25 years to investigate the potential effects of repeated vaccinations. The participants underwent physical health examinations and laboratory testing in 1956, 1962, and 1971. No health problems due to intense long-term immunization could be identified in this group. None of the subjects suffered unexplained

clinical symptoms requiring them to take sick leave that could be caused by the vaccination program.

There was some evidence of a chronic inflammatory (local swelling) response, as characterized by certain laboratory test abnormalities. However, these changes cannot necessarily be attributed to the vaccinations, because the workers studied were exposed to many environmental hazards in their work. This series of on-going health studies had several problems. However, the studies were valuable because careful monitoring did not disclose any evidence of serious unexplained illness in a group that received a series of intense vaccinations over many years.

Several studies of British Gulf War veterans provide some limited evidence of an association between multiple vaccinations and long-term multi-symptom health problems, especially for vaccinations given during deployment. There are some limitations and confusing issues with these studies, and further research is needed.

The IOM committee concluded that there is inadequate/insufficient evidence to determine whether an association does or does not exist between multiple vaccinations and long-term adverse health effects.