



RESEARCH ON GULF WAR VETERANS' ILLNESSES

VA Research is conducting a wide array of studies to better understand and treat the illnesses experienced by some Veterans of the 1990–1991 Gulf War.

Nearly 700,000 men and women served in the Persian Gulf during operations Desert Storm and Desert Shield in 1990 and 1991, and studies show that at least a quarter continue to report troubling health symptoms that are not easily diagnosed.

The majority of these Veterans are considered to have what VA terms “medically unexplained chronic multi-symptom illness.” Others are considered to have chronic fatigue syndrome, fibromyalgia, functional gastrointestinal disorders, or undiagnosed illnesses. VA has established a presumptive Gulf War service connection for the above-mentioned conditions, as well as for a number of infectious diseases, provided certain conditions apply.

Our mission, as it relates to Gulf War Veterans, is to learn more about these illnesses and identify the best ways to diagnose and treat them. The overarching goal is to improve the health and well-being of those who served in the Gulf and continue to experience health problems.

VA’s efforts are guided by a Strategic Plan for Gulf War Research. The plan was developed with input from leading scientists and researchers in the area of Gulf War research, physicians, and Veterans themselves. The plan will be reviewed annually to make sure it incorporates the latest emerging knowledge.

Along with the specific topics and goals outlined in the Strategic Plan, VA investigators are conducting research in many other areas that may be relevant to Gulf War Veterans, even if the studies are focused on broader patient populations. Examples include studies on pain, autoimmune disease, neurodegenerative disease, sleep disorders, gastrointestinal disorders, respiratory problems, and other chronic diseases.

All of this work relies on the talents and hard work of VA investigators nationwide, and their research partners. Just as essential are the dedication and altruism of the many Gulf War Veterans and others who participate in this research as volunteers. VA’s vision is that these efforts will not only directly improve the health and well-being of thousands of Gulf War Veterans, but also create a healthier tomorrow for future generations of Service members and Veterans.





VA Research aims to improve the health and well-being of those who served in the Gulf and continue to experience health problems.

Epidemiological Studies: What Do We Know about Gulf War Veterans' Health?

Numerous studies by VA researchers and others have shown that men and women deployed to the Persian Gulf during operations Desert Storm and Desert Shield in 1990–1991 reported, and continue to report, health problems at higher rates than those who were not deployed. Common symptoms have included headaches, joint and muscle pain, fatigue, attention and memory difficulty, indigestion, sleep disturbances, respiratory problems, and skin abnormalities. Some of the Veterans reporting health problems meet the diagnostic criteria for chronic fatigue syndrome, fibromyalgia, or certain other known disorders. Most, however, have what VA terms “medically unexplained chronic multisymptom illnesses.”

Most notably, the “Longitudinal Health Study of Gulf War Era Veterans,” conducted by VA, is one of the largest studies on the health of Gulf War Veterans. This study has compared changes in the health of 1990-1991 deployed Gulf War Veterans to Veterans not deployed to the Gulf. Researchers conducted a baseline survey in 1995, conducted a follow-up survey in 2005, and are now planning to survey this group of Veterans a third time.

Results from the 2005 follow-up appeared in late 2011 in the *American Journal of Epidemiology*. The report compared changes in health between 1995 and 2005 among nearly 9,000 deployed and non-deployed Veterans of the Gulf era. The study confirmed and extended

earlier findings: Deployed Veterans were more likely than non-deployed Veterans to report new health problems and greater persistence of existing illnesses. Differences between the groups were seen in areas such as limitation of daily activities, repeated clinic visits, recurrent hospitalizations, self-perceived health status, and chronic fatigue and posttraumatic stress symptoms.

VA continues to support epidemiological research dedicated to understanding chronic multi-symptom illnesses and the long-term health effects of potentially hazardous substances to which Gulf War Veterans may have been exposed, such as depleted uranium or smoke from oil well fires.

Longer-term plans include a new genetic study of Gulf War Veterans. The effort entails the collection of survey data and the banking of blood in a “biorepository” to better understand genetic influences on Gulf War illnesses and responses to treatments. This study, like other VA research in this area, is guided by Institute of Medicine reports; recommendations from the Research Advisory Committee on Gulf War Veterans’ Illnesses (www.va.gov/rac-gwvi) and the National Research Advisory Council (www.va.gov/advisory/nrac.asp); and rigorous evaluations of the existing scientific and medical literature.

Planning Gulf War Research: Engaging with Internal and External Partners

To address the health problems that still affect Veterans of the 1990-1991 Gulf War, VA has developed a Gulf War Research Strategic Plan. The plan was developed in 2012 with the help of advisory committee members, Gulf War researchers, Gulf War Veterans, and other stakeholders. These individuals contributed suggestions on future research directions and areas of emphasis.

Members of the Research Advisory Committee on Gulf War Veterans' Illnesses and the National Research Advisory Council either took part in the working groups or recommended others for inclusion. The working groups included more than 40 people in all.

Importantly, the process by which the plan was developed was transparent and open to the public, via open meetings and minutes from all discussions posted on the advisory committees' websites. The great majority of the working groups' suggestions were incorporated into the plan with no change or modified only slightly. Some suggestions had to be modified or deleted because they were beyond the scope of a strategic plan for research, or because they did not conform to federal law or VA policy.

The main focus of the Strategic Plan is the health of Gulf War Veterans. While the plan comprehensively addresses a range of issues related to Gulf War research, it strongly emphasizes the need for effective treatments for the symptoms experienced by these Veterans. As stated in the plan, **"The most urgently needed Gulf War research studies are those that advance identification of effective treatments that can substantially improve Veterans' health and quality of life, and this is the focus of the Gulf War research portfolio."**

The Strategic Plan will be reviewed annually to make sure it continues to effectively address the needs and concerns of Gulf War Veterans.

Also of note is the Gulf War Veterans Illnesses' Task Force. This group is concerned with every aspect of a Gulf War Veteran's experience within VA. The group's latest report was released in March 2012 and is available at www.va.gov/opa/publications/2011_GWVI-TF_Report.pdf. A preliminary draft of the report had been posted on the Web to allow interested parties to comment. This direct feedback helps VA ensure that its activities are aligned with the medical needs of Veterans.



Finding the Best Treatments to Help Gulf War Veterans

The overarching focus of VA's Gulf War research is finding treatments that effectively address the symptoms experienced by many Gulf War Veterans.

One recent study, based at the Northport, NY, VA Medical Center, found that 96 percent of Veterans with chronic multisymptom illness experienced breathing problems during sleep. In contrast, only 36 percent of Gulf War Veterans without multisymptom illness experienced this problem. The study also showed that a therapy known as nasal continuous positive airway pressure (CPAP) can ease breathing and sleep problems. Some Veterans receiving the CPAP therapy also reported reductions in pain and fatigue, along with improvements in cognitive function, sleep quality, and general health. This pilot study is being expanded so researchers can better understand the potential benefits of CPAP therapy for Gulf War Veterans.

Other studies are addressing the chronic pain and cognitive and memory issues that affect many Gulf War Veterans.

One study is looking at resistance exercise training as a treatment for chronic muscle and joint pain.

Pain symptoms, changes in physical activity, and the overall well-being of patients—including sleep problems, fatigue, anxiety, and depression—are being evaluated through various measures, including MRI studies of the brain's pain centers. The expected outcome is that patients receiving the therapy will have reduced pain and better physical function. The researchers also expect to show the value of MRI as both a diagnostic test and a way to monitor patients' progress and well-being.

Another ongoing study has linked exposure to some of the same chemicals that were present in the Persian Gulf region in 1990–1991 with cognitive and memory problems, and with changes in a region of the brain known as the hippocampus. The next phase of the study, now under way, involves treatments with a combination of drugs that could help repair the hippocampus.

In other research, investigators are exploring whether repetitive transcranial magnetic stimulation can treat

chronic pain in Gulf War Veterans. This therapy uses brief pulses of a magnetic field to non-invasively stimulate areas of the brain. It has been found safe and effective in treating patients with depression or stroke, and researchers in VA and elsewhere have been exploring other potential applications.

Some work that is funded by VA to help Gulf War Veterans involves approaches rooted in complementary and alternative medicine, or integrative medicine. One example is a study at the Puget Sound VA Healthcare System. Researchers are testing a well-validated approach known as Mindfulness-Based Stress Reduction (MBSR). Up to 60 Gulf War Veterans with chronic multisymptom illness will complete an eight-week MBSR course, and researchers will evaluate the effects on pain, fatigue, cognitive function, attention, and memory. Yoga and acupuncture are among the other therapies being explored at other sites.



Also, studies in many additional areas of research may yield important new knowledge to help Gulf War Veterans, along with Veterans of other eras. These topic areas include pain, muscle and bone disorders, autoimmune disease, neurodegenerative disease, sleep disorders, gastrointestinal disorders, respiratory problems, or other chronic diseases.

VA also recognizes the importance of studying other conditions that may affect Gulf War Veterans, such as brain cancer, amyotrophic lateral sclerosis (Lou Gehrig's disease, or ALS), and multiple sclerosis. VA maintains very active research portfolios in each of these areas, with the aim of improving life for Veterans of any era who may be affected.

Improving Diagnostic Methods

VA researchers are working to develop new methods for diagnosing the chronic multisymptom illness that affects so many Gulf War Veterans. Efforts are also under way to better define the condition—based on the latest evidence—and distinguish it from other known conditions that may have some symptoms in common.

Toward this end, VA is funding research aimed at better understanding the genetic, physiological, and other biological factors underlying Gulf War Veterans' illnesses. This will enable scientists to identify reliable biomarkers—an important step toward improved diagnosis.

In one study, based at the Center for Imaging of Neurodegenerative Disease at the San Francisco VA Medical Center, researchers used magnetic resonance imaging (MRI) to compare two groups of Veterans—one made up of Gulf War Veterans who were likely exposed to organophosphate chemicals—namely, the chemical warfare agents sarin and cyclosarin—and the other composed of Veterans who were not exposed. The imaging study identified brain differences between the two groups. While more testing needs to be done, this approach may lead to a reliable method for identifying Veterans with chronic multisymptom illness.

The San Francisco study added to earlier findings, from a team at the Boston VA Healthcare System, showing “subtle but persistent central nervous system pathology in Gulf War Veterans potentially exposed to low levels of sarin/cyclosarin.”

The San Francisco group has also found differences in the size of the hippocampus—a brain region critical in memory and learning—in Gulf War Veterans with a diagnosis of posttraumatic stress disorder.

The same researchers are now conducting further MRI studies comparing the levels of an important brain chemical—N-acetylaspartate—in the brains of Gulf War Veterans with and without chronic multisymptom illness.

Other new studies are using a relatively new imaging technique called magnetoencephalography (MEG) to study how the brain works. MEG detects very weak magnetic signals produced by brain cells. Studying these signals can help determine which parts of the brain are functioning normally and which are not. The goal is to identify certain signature patterns that may identify those with chronic multisymptom illness. This work, based at the Minneapolis VA Medical Center, is supported in part by the American Legion.



BIOMARKERS OF GULF WAR VETERANS' ILLNESSES

Some Gulf War research conducted by VA scientists is supported through the Department of Defense and the Congressionally Directed Medical Research Program. This research includes the following two promising studies of potential biomarkers:



Dr. Ronald Bach of the Minneapolis VA Medical Center is examining the level of a protein called “tissue factor” in blood samples from Gulf War Veterans. The protein promotes healthy clotting. Too much of it, however, can restrict blood flow in small blood vessels throughout the

body. Over time, this can lead to symptoms such as pain, fatigue, and slowed thinking—all associated with Gulf War Veterans' health problems. Dr. Bach's team, which also has funding from VA, is also measuring other proteins linked to coagulation, as well as to inflammation. The researchers hope their analysis will uncover new biomarkers for Gulf War Veterans' illnesses.

Dr. Maxine Krengel, with VA and Boston University, and colleagues are using magnetic resonance images of the brain and neuropsychological testing to explore the possible long-term neurological effects of toxic substances to which some Gulf War Veterans were exposed. One category of substances includes pesticides that inhibit an enzyme called acetylcholinesterase, important for proper brain function. Another substance is a drug that was used to protect against nerve gas, known as pyridostigmine bromide, or PB. Some Service members were doubly exposed: They worked with or around pesticides and took PB tablets. Participants in the study include Veterans who were exposed at varying levels to both substances. The work could yield important new knowledge to help researchers understand the causes of Gulf War Veterans' illnesses and develop new therapies.

Supporting High-Quality Research and Translating Findings Into Care

In addition to providing administrative support to help VA investigators plan and carry out high-quality research, VA has begun collections of blood samples and patient information from Gulf War Veterans that will be made available to researchers as appropriate, with stringent privacy safeguards in place. These blood samples will help researchers find genetic factors that might be related to Veterans' illnesses. Participation in these specimen banks by Gulf War Veterans is completely voluntary. Veterans who choose to participate realize that their efforts are essential for this research to succeed.

VA is holding in-person meetings and teleconferences in fall 2012 to disseminate information about the new Gulf War Research Strategic Plan, and the related Implementation Plan, among VA investigators. The goal is to encourage investigators to pursue studies aimed at improving the health of Gulf War Veterans.

VA is also supporting Gulf War studies through a "virtual," Web-based Gulf War treatment-research coordinating process to assist researchers in conducting treatment trials and to track their progress. Other measures VA is taking to promote Gulf War research include providing incentive awards to supplement investigators' research budgets, and funding follow-up studies on promising results from small-scale or preliminary studies.

Importantly, VA has in place a number of programs and initiatives to promote the translation of research results into everyday clinical care. One of the ways VA plans to foster the translation of Gulf War research results into practice is the dissemination of significant findings to clinicians at VA's War-Related Illness and Injury Study Center. This center, which provides services nationwide through its three sites, in New Jersey, Washington, DC, and California, specializes in helping Veterans with post-deployment health concerns, especially those involving difficult-to-diagnose or medically unexplained symptoms and environmental exposure concerns.



One Veteran's Story

DANIEL STEBBINS served in the Marine Corps from 1986 to 1991 as an infantryman, specializing in heavy weapons. He served in operations Desert Shield and Desert Storm and stayed with his Marine Corps unit in Kuwait for about a year after the fighting had ended, patrolling the highways between Iraq and Kuwait.

Suffering from chronic multisymptom illness, Stebbins began seeking VA care in 2000. **"I couldn't do many of the things I used to do without literally sitting down and being out of energy,"** he said. **"I was in denial [about the health issues] for a long time."**

Through his VA medical center, Stebbins was informed that he would be a good candidate for a sleep study being conducted for Gulf War Veterans. The study tested the benefits of a therapy known as continuous positive airway pressure (CPAP). Patients receiving CPAP treatment



Daniel Stebbins in an abandoned Iraqi tank.

wear a special mask while sleeping that produces mild air pressure to keep the airways open.

Stebbins noticed improvements from the therapy: more restful sleep throughout the night, and more energy and alertness and better concentration and performance during the day.

Stebbins added, **"I have seen benefits from the research study and feel I'm doing something good for my fellow Veterans through participating in VA research."**



FOR MORE INFORMATION

National Research Advisory Council
www.va.gov/advisory/nrac.asp

Research Advisory Committee on Gulf War Veterans' Illnesses
www.va.gov/rac_gwvi

War Related Illness and Injury Study Center
www.warrelatedillness.va.gov

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