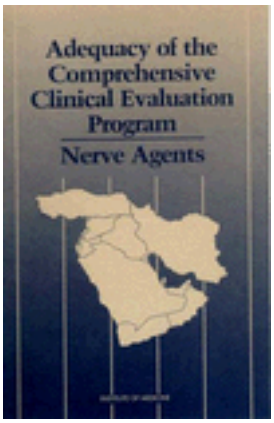

Adequacy of the Comprehensive Clinical Evaluation Program: Nerve Agents

Committee on the Evaluation of the Department of Defense Comprehensive Clinical Evaluation Program, Institute of Medicine

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Adequacy of the Comprehensive Clinical Evaluation Program

Nerve Agents

Committee on the Evaluation of the Department of Defense
Comprehensive Clinical Evaluation Program
Division of Health Promotion and Disease Prevention
INSTITUTE OF MEDICINE

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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatlichemuseen in Berlin.

COMMITTEE ON THE EVALUATION OF THE DoD COMPREHENSIVE CLINICAL EVALUATION PROGRAM

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Contents

Executive Summary

On August 2, 1990, Iraq invaded Kuwait and the Persian Gulf War began. The United States deployed almost 700,000 military personnel to the Gulf in Operations Desert Shield and Desert Storm. Following a brief war, most troops returned home and resumed their normal activities. Some, however, began to report various health problems that they believed were related to their deployment in the Persian Gulf. As reports of a purported "Persian Gulf Illness" circulated, public concern grew. In response, the Department of Veterans Affairs (VA) and the Department of Defense (DoD) developed a registry and clinical programs to track the health of Persian Gulf veterans.

The Comprehensive Clinical Evaluation Program (CCEP) was developed by the DoD to provide a systematic clinical evaluation program for the diagnosis and treatment of active-duty military personnel who have medical complaints they believe could be related to their service in the Persian Gulf. Since the program began, about 28,600 active duty Persian Gulf veterans have requested clinical examinations. By December 31, 1996, 24,400 veterans had received completed evaluations; an additional 4,180 are currently involved in some phase of the examination process.

In 1994, the DoD asked the Institute of Medicine to convene a committee to evaluate the adequacy of the CCEP. This committee reached the conclusion that the CCEP is a comprehensive effort to address the clinical needs of the thousands of active-duty personnel who served in the Gulf War. In addition, the committee found that, although the CCEP is not appropriate as a research tool, the results could and should be used to: educate Persian Gulf veterans and the physicians caring for them; improve the medical protocol itself; and evaluate patient outcomes.

The DoD asked the Institute to continue its evaluation of the CCEP with special attention to three issues: (1) approaches to addressing difficult-to-diagnose individuals and those with ill-defined conditions; (2) the diagnosis and treatment of stress and psychiatric conditions; and (3) the assessment of health problems of those who may have been exposed to low levels of nerve agents. This new committee (CCEP 2) was also asked to consider whether there are medical tests or consultations that should be added to the CCEP to increase its diagnostic yield. The following diagram describes the output of the two CCEP committees.

CCEP 1 →	CCEP 1 →	CCEP 1 →	CCEP 2 →	CCEP 2
First Report Released December 1994	Second Report Released August 1995	Final Report Released January 1996	First Report Released April 1997	Final Report Anticipated October 1997

Because of growing concern about the health problems of those veterans who may have been exposed to low levels of nerve agents, the DoD asked the committee to address this issue first. A 1-day workshop was held during which leading researchers and clinicians presented the latest scientific and clinical information regarding possible health effects of low-level exposure to nerve agents and chemically related compounds, as well as the tests available to measure the potential health effects of such exposures. Because there is little available research documenting long-term health effects of low-level exposure to nerve agents, speakers were asked to address the kinds of effects that *might* exist. These potential effects included neurological problems such as peripheral sensory neuropathies and psychiatric effects such as alterations in mood, cognition, or behavior.

The committee concluded that, overall, the CCEP provides an appropriate screening approach to the diagnosis of a wide spectrum of neurological diseases and conditions. The issue of psychological and psychiatric problems will be addressed in greater detail in the upcoming workshops and the final committee report.

The committee agreed that, given the possibility of low-level exposure to nerve agents, certain refinements in the CCEP would enhance its value. Although these refinements need not be applied retrospectively, the committee hopes implementation will be rapid so that as many new enrollees as possible will benefit from the improved system. Refinements include:

- improved documentation of the screening used during Phase I for patients with psychological conditions such as depression and posttraumatic stress disorder (PTSD);
- improved documentation of neurological screening used during both Phase I and Phase II of the CCEP;

- ensuring that Phase I primary physicians have ready access to a referral neurologist and a referral psychiatrist;
- ensuring that more complete histories are taken, particularly regarding personal and family histories, the onset of health problems, and the occupational and environmental exposures for each patient;
- standardization—to the extent possible—of predeployment physical examinations given members of the armed forces across the services;
- increased uniformity of CCEP forms and reporting procedures across sites;
- for each patient, the physician should provide written evidence that all organ systems were evaluated; and
- DoD should offer group education and counseling to soldiers and their families concerned about exposure to toxic agents.

The committee emphasizes that the CCEP is *not* an appropriate vehicle for addressing questions about the possible long-term health effects of low-level exposure to nerve agents. Those questions must be addressed through rigorous scientific research. The CCEP is a treatment program. Therefore, it is important not to attempt to use the findings of the CCEP to answer research questions. The committee believes strongly that although data from the CCEP cannot be used to test for potential associations between exposures and health effects, it can, combined with other information, be used to identify promising directions for separate research studies.

Introduction

A large Iraqi force invaded the independent nation of Kuwait on August 2, 1990. Within 5 days, the United States began deploying troops to the Persian Gulf in Operation Desert Shield. On January 16, 1991, UN coalition forces began intense air attacks against the Iraqi forces (Operation Desert Storm). By February 1991, more than 500,000 US troops were present and ready to engage the Iraqi army. A ground attack was launched on February 24, and within 4 days Iraqi resistance crumbled. After the fighting, the number of US troops in the area began to decline rapidly. By June 1991, fewer than 50,000 US troops remained.

Almost 700,000 US troops participated in Operations Desert Shield and Desert Storm. The composition of these troops differed from any previous US armed force. Overall, they were older, a large proportion (about 17%) were from National Guard and Reserve units, and almost 7% of the total forces were women.

US casualties were low during the Persian Gulf War. There were 148 combat deaths, with an additional 145 deaths due to disease or accidents. Despite the low number of fatalities and injuries, service personnel in the Persian Gulf were exposed to a number of stresses. These included environmental factors such as pesticides, diesel fumes, microbes, and oil well fires; and psychosocial factors such as the sudden mobilization for military service (especially for military reserves), the different cultural traditions of the region, and the primitive living conditions into which some troops were placed.

Following the war, most troops returned home and resumed their normal activities. However, a number of active-duty military personnel and veterans have reported various health problems they believe are connected to their Persian Gulf deployment. Symptoms commonly described include fatigue, memory loss, severe headaches, muscle and joint pain, and rashes (Iowa Persian Gulf Study Group, 1997). As reports of a purported "Persian Gulf Illness"

circulated, public concern grew. Both the Department of Defense (DoD) and the Department of Veterans Affairs (VA) developed a registry to track the health of Persian Gulf veterans and clinical programs to diagnose and treat program participants. In June 1994, the DoD instituted the Comprehensive Clinical Evaluation Program (CCEP), the purpose of which is to diagnose and treat active-duty military personnel who have medical complaints they attribute to service in the Gulf.

In 1994, the DoD asked the Institute of Medicine (IOM) to assemble a group of medical and public health experts to evaluate the adequacy of the CCEP. This committee met four times and prepared three reports between October 1994 and January 1996 (IOM 1995, 1996a,b). A general discussion of this committee's findings appears in the section entitled, "CCEP: The Initial IOM Report" (page 8). A complete list of the first CCEP committee's recommendations appears in Appendix A. Given these recommendations and an analysis by the DoD of information derived from the CCEP, the IOM was asked to continue its review of the CCEP with special emphasis on three areas: (1) approaches to addressing individuals with difficult-to-diagnose or ill-defined conditions, (2) diagnosis and treatment of stress and psychological or psychiatric conditions, and (3) identifying health problems of those who may have been exposed to nerve agents.

Given the intense interest in and concern about the potential health effects of possible exposure to nerve agents, DoD asked the committee to focus first on addressing the health problems of those who may have been exposed to such agents. To do so, a 1-day workshop was held at which leading researchers and clinicians presented the latest scientific and clinical information regarding possible health effects of low-level exposure to nerve agents and chemically related compounds, as well as the tests available to measure the potential health effects of such exposures.

The Comprehensive Clinical Evaluation Program*

OVERVIEW

In June 1994 the DoD instituted the CCEP to provide a thorough systematic clinical evaluation program for the diagnosis and treatment of Persian Gulf veterans at military facilities in the US and overseas. Since then, more than 37,800 veterans (of whom about 13% are women) have enrolled in the CCEP registry. Of those, about 28,580 (about 12% of whom are women) have requested clinical examinations. By December 31, 1996, 24,400 veterans (or about 12% of those eligible) had received completed evaluations, while an additional 4,180 are currently involved in some phase of the examination process.

The CCEP was designed to: (1) strengthen the coordination between the DoD and the VA; (2) streamline patient access to medical care; (3) make clinical diagnoses in order to treat patients; (4) provide a standardized, staged evaluation and treatment program; and (5) assess possible Gulf War-related conditions. (Veterans who have left military service entirely are eligible for evaluations from the VA; personnel still on active duty, in the Reserves, or in the National Guard may request medical evaluations from DoD.) Phase I of the CCEP consists of a medical history, physical examinations, and laboratory tests. These are comparable in scope and thoroughness to an evaluation conducted during an in-patient internal medicine hospital admission (see Appendix B). All CCEP participants are evaluated by a primary care physician at their local medical treatment facility and receive specialty consultations if they are deemed

* Portions of this section are based upon workshop presentations by Anthony Amato, M.D.; Col. Ray Chung; Lt. Col. Tim Cooper; Capt. Andrew Dutka; Maj. Chuck Engel; Lt. Col. Robert Gum; and Col. Kurt Kroenke.

appropriate by their primary care physician. Evaluation at this phase includes a survey for nonspecific patient symptoms, including fatigue, joint pain, diarrhea, difficulty concentrating, memory and sleep disturbances, and rashes.

The primary care physician may refer patients to Phase II for further specialty consultations if he or she determines it is clinically indicated. These Phase II evaluations are conducted at a regional medical center and consist of targeted, symptom-specific examinations, lab tests, and consultations. During this phase potential causes of unexplained illnesses are assessed, including infectious agents, environmental exposures, social and psychological factors, and vaccines and other protective agents. Both Phase I and Phase II are intended to be thorough for each individual patient and to be consistent among patients.

Every medical treatment facility has a designated CCEP physician coordinator who is a board-certified family practitioner or internal medicine specialist. The coordinator is responsible for overseeing both the comprehensiveness and quality of Phase I exams. At regional medical centers CCEP activities are coordinated by board-certified internal medicine specialists who also oversee the program operations of the medical treatment facilities in their region.

In March 1995, the DoD established the Specialized Care Center at Walter Reed Army Medical Center to provide additional evaluation, treatment, and rehabilitation for patients who are suffering from chronic debilitating symptoms. A small select group of patients have been referred from regional medical centers to the Specialized Care Center for an intensive 3-week evaluation and treatment program designed to improve their health status.

IMPLEMENTATION

The DoD has summarized the information obtained through the CCEP in reports released to the public. In the most recent published report, which covered 18,598 participants seen through December 6, 1995, the most frequent primary diagnoses were psychological conditions (18.4%); musculoskeletal conditions and connective tissue diseases (18.3%); symptoms, signs, and ill-defined conditions (17.9%); respiratory diseases (6.8%); and digestive system diseases (6.3%). An additional 9.7% were found to be healthy.

When both primary and secondary diagnoses were considered, the most common diagnostic categories were musculoskeletal diseases (47.2%); symptoms, signs, and ill-defined conditions (43.1%); psychological conditions (36.0%); digestive diseases (17.5%); and nervous system diseases (17.8%) (CCEP report on 18,598 participants, April 2, 1996).

The most frequently recorded psychological diagnoses were tension headache, depression, anxiety disorders, adjustment reactions, and somatoform disorders. For participants with a primary diagnosis of symptoms, signs, and ill

defined conditions, the most common conditions were malaise and fatigue (26.6%), sleep disturbance (17.7%), and/or headache (15.3%). More than 50% of the patients with a primary diagnosis of musculoskeletal and connective tissue conditions had pain in joints, osteoarthrosis, and backache.

Five percent of the participants in the CCEP had a primary diagnosis of a neurological disorder. In addition, 11.8% of all participants were diagnosed with at least one neurological condition. The most common primary neurological diagnosis was migraine headache (56%) followed by carpal tunnel syndrome (9.5%), other peripheral mononeuropathies (0.25%), and benign essential tremors (2.3%) (DoD, 1996: 68).

Major neuromuscular complaints recorded during Phase I included myalgias, fatigue and weakness. Patients who complained of severe muscle weakness, fatigue, or myalgias that lasted at least 6 months and interfered with normal functioning were referred to neuromuscular specialists for evaluation. At a minimum, these patients had median and sural sensory nerve action potentials recorded. Additional tests were ordered as deemed necessary by the neurologist. After extensive clinical, electrophysiological, and histological testing, no significant, objective neuromuscular pathology was identified that would suggest a possibly distinct neuromuscular disorder in these patients.

CCEP: THE INITIAL IOM REPORT

In July 1994, Dr. Stephen Joseph, Assistant Secretary of Defense for Health Affairs, asked the IOM to convene a committee to evaluate the clinical assessments of the CCEP and to comment on the interpretation of its results to date. That committee was also asked to make recommendations regarding how the clinical assessments should be conducted in the future and on DoD's broader program of Persian Gulf health studies. Committee members included experts in general medicine, occupational and environmental medicine, rheumatology, infectious disease, psychiatry, psychology, and clinical neurotoxicology. The committee reached the following conclusions (for a complete set of recommendations of the first CCEP committee, as well as a list of committee members, see Appendix A):

- The CCEP is a comprehensive effort to address the clinical needs of thousands of active-duty personnel who served in the Gulf War. The CCEP leads to a specific medical diagnosis or diagnoses for most patients. The DoD has made conscientious efforts to build consistency and quality assurance into this program at the many medical treatment facilities and regional medical centers across the country.
- DoD efforts to compare the symptoms and diagnoses in the CCEP with those in several community-based and clinically based populations "should be

made with great caution and only with the explicit recognition of the limitations of the CCEP as a self-selected case series. The CCEP results do have considerable clinical utility, and they could be used to address many important questions from a descriptive perspective."

- "The results of the CCEP can and should be used for several purposes, including (1) educating Persian Gulf veterans and the physicians caring for them, (2) improving the medical protocol itself, and (3) evaluating patient outcomes. The medical findings of the CCEP should be distributed promptly to all CCEP primary care physicians." These findings would also be of "considerable value and interest to physicians in the VA system and in the community."
- "DoD should consider developing a comprehensive document for use in the CCEP that describes the potential physical, chemical, biological, and psychological stressors that were present in the Persian Gulf theater. If the CCEP physicians could obtain a clearer picture of the possible range of exposures, they might be able to counsel their patients more effectively."
- DoD has taken a serious approach to the treatment and rehabilitation of patients who have treatable, chronic diseases. If the Specialized Care Center "program is successful in improving the health and functional status of its patients, perhaps the elements that are most effective in enabling the patients to cope with their symptoms could be identified. It might then be possible to disseminate some of these elements to the DoD medical treatment facilities, which are close to where the CCEP patients live and work."

CCEP: IOM REVIEW CONTINUED

Late in 1995, the DoD asked the IOM to continue its evaluation of the CCEP with special attention to two issues: (1) difficult-to-diagnose individuals and those with ill-defined conditions; and (2) the diagnosis and treatment of patients with stress and psychiatric conditions. A new committee was convened to address these issues. Most members of the newly formed committee were also members of the first IOM CCEP committee.

With the disclosure in June of 1996 that some US ground troops may have been exposed to low levels of nerve agents following the destruction of the munitions dump at Khamisiyah, the DoD asked the IOM to add to its assessment whether the present CCEP protocol is adequate for evaluating the health of individuals who may have been exposed to low levels of nerve agents.

In defining the tasks included in Phase II, it is important to note what is *not* included in the committee's charge. It is *not* this committee's charge to determine whether or not there is such an entity (or entities) as "Persian Gulf Illness." It is *not* this committee's charge to determine whether or not there are

long-term health effects from low-level exposure to nerve agents. These questions are more properly the subject for extensive scientific research.

The committee charge, then, is threefold. It is to evaluate the adequacy of the Dolls Comprehensive Clinical Evaluation Program regarding:

- approaches to dealing with difficult-to-diagnose individuals and those with no diagnosis, as well as poorly defined conditions such as chronic fatigue syndrome, fibromyalgia, and multiple-chemical sensitivity;
- the diagnosis and treatment of stress and psychiatric conditions, the relationship between stress and psychiatric conditions and physical symptoms, and predeployment screening and mitigation of stressors in future deployments; and
- assessment of the health problems of those who may have been exposed to low levels of nerve agents.

The committee also will consider whether there are medical tests or consultations that should be systematically added to the CCEP to increase its diagnostic yield.

A series of workshops was planned to obtain information on these topics. Given the urgency surrounding the question of health problems of those who may have been exposed to low levels of nerve agents, DoD asked the Committee to address this topic first. A 1-day workshop was held on December 3, 1996, during which information was gathered from leading researchers and clinicians about effects of exposure to nerve agents and chemically related compounds, as well as about tests available to measure potential health effects of such exposures. (See Appendix C for the workshop agenda and list of speakers.) The committee spent the day following the workshop examining and analyzing this information in detail in order to develop its recommendations.

Testing for and Identifying Health Effects of Exposure to Nerve Agents*

Nerve agents are extremely toxic compounds that were designed specifically to kill or incapacitate. Sarin and cyclosarin (the agents of concern in the Persian Gulf) are organophosphates that permanently inhibit acetylcholinesterase. This results in an accumulation of acetycholine at the cholinergic synapses, causing continued stimulation of the affected organ. The toxic effects of poisoning depend largely on the intensity of exposure. The effects range from miosis, or pinpoint pupils, and blurred vision at lower concentrations, to involuntary defecation, nausea, vomiting, muscular twitching, weakness and convulsions, and death at somewhat higher concentrations.

Experimental studies on the long-term effects of sarin on animals and humans have produced inconclusive results. In 1982, the National Research Council conducted a study examining long-term or delayed adverse health effects of 15 anticholinesterases tested on about 1,400 military volunteers during the 1960s and 1970s. That panel concluded that "although no evidence has been developed (to date) that any of the anticholinesterase test compounds surveyed carries long-range adverse human health effects in the doses used, the panel is unable to rule out the possibility that some anti-ChE [cholinesterase] agents produced long-term adverse health effects in some individuals. Exposures to low doses of OP [organophosphate] compounds have been reported (but not confirmed) to produce subtle changes in EEG, sleep pattern, and behavior that lasts for at least a year." (NRC, 1982: 33).

* The material in this section is based, in part, upon presentations and discussion by Kent Anger, Ph.D.; Arthur Asbury, M.D.; David Cornblath, M.D.; Bhupendra Doctor, M.D.; Eva Feldman, M.D.; Lt. Col. Robert Gum, M.D.; David Janowsky, M.D.; Richard Johnson, M.D.; Robert MacPhail, Ph.D.; Peter Spencer, Ph.D.; and Roberta White, Ph.D.

Lack of knowledge regarding who might have been exposed to nerve agents and at what level is impeding researchers attempting to answer questions about health effects. The extent and frequency of exposure of troops to nerve agents in the Persian Gulf is still being investigated. Concerns about exposure were heightened by the announcement that troops in the vicinity of Khamisiyah on March 10, 1991, may have been exposed to sarin or cyclosarin when US military personnel destroyed a munitions dump. It is not known whether or to what extent personnel were exposed. In addition, the military is investigating other potential exposures to nerve agents in the Persian Gulf. Without definitive information on the intensity and frequency of exposures, interpretation of research results is problematic.

Research on exposure to organophosphate pesticides, some of the most acutely toxic and potentially lethal pesticides in use today, may provide information useful to those studying the effects of sarin and cyclosarin because these types of pesticides and nerve agents both inhibit cholinesterase. Acute symptoms of poisoning from these OP pesticides can be as severe as those found with any nerve agent, but the long-term neurobehavioral health effects in the absence of acute clinical effects at the time of exposure are still debated

A study of individuals occupationally exposed to organophosphate pesticides examined workers without acute, clinical symptoms, but with blood measurements that showed depressed cholinesterase levels. Neurobehavioral tests were used in the study but no residual neurologic health effects were documented in this population (Ames et al., 1995).

Detection, over time, of organophosphate nerve agents in the blood is impossible because such agents are completely detoxified by a set of enzymes in the body. Therefore, measuring the presence of nerve agents in the blood over time is not a practical approach for determining whether an exposure occurred. In addition, there is no surrogate marker of exposure.

Another important issue is the use of pyridostigmine bromide (PB) pills which were distributed to soldiers deployed to the Persian Gulf. Pyridostigmine bromide is a carbamate that also inhibits acetylcholinesterase. Unlike sarin and cyclosarin, however, PB binds *temporarily* with acetylcholinesterase. The DoD's intent, therefore, was for troops threatened with exposure to chemical warfare agents to take the pills so the PB could bind temporarily with their acetylcholinesterase, leaving little available for the nerve agents to act on. Any acute clinical response to PB would be short-lived, unlike responses to sarin and cyclosarin, thereby saving the life of the exposed victim. Acute, short-term effects of PB can include respiratory problems, nausea, and diarrhea. As is the case with sarin and cyclosarin, there has been little research into the long-term health effects of PB used in healthy individuals exposed to low levels of nerve agents.

Long-term health effects of low level nerve agent exposure have not been shown to exist. However, it might be hypothesized that such health effects, if they exist, might relate to inhibition of acetylcholinesterase and be manifested as

neurological problems (e.g., peripheral sensory neuropathies) and as psychiatric problems (e.g., alterations in mood, cognition or behavior). Persons who may have been exposed to nerve agents could, therefore, be examined for both junctional myopathies and peripheral neuropathies. Junctional myopathy is normally associated with life-threatening respiratory muscle damage, not with acute anticholinesterase effects. Organophosphate-induced junctional myopathies are thought to be caused by excessive acetylcholine activity at the neuromuscular junction, whereas peripheral neuropathies are thought to be caused by inhibition of an enzyme known as neuropathy target esterase.

Toxic insults can damage nerve axons, resulting in subsequent loss of nerve fiber and the development of neuropathy. Symptoms of neuropathy include numbness, tingling, and prickling sensations with differing degrees of intensity and duration. Signs of neuropathy include mild loss of vibration at toes, decreased ankle reflexes early on, and sensory loss later. A conventional neuropathy diagnosis begins with a careful patient history, followed by a characterization of the symptoms and electrophysiological tests. These tests traditionally involve nerve conduction studies and quantitative sensory testing. Severe neuropathy may extend to the central nervous system, leading to more critical problems.

An accurate, etiologic diagnosis of a neuropathy cannot be based on symptoms alone. A simple, reliable neuropathy diagnosis requires a neurologist, a set of noninvasive diagnostic instruments including a thorough patient history questionnaire; clinical examination questions about sensory, motor, and autonomical functions; and simple nerve conduction and quantitative sensory tests. In addition, physicians must consider other possible etiologies of neuropathy in patients, including inherited problems, paraneoplastic syndromes, immune-mediated neuropathy, infectious vectors including HIV status, diabetes, alcohol use, and the use of therapeutic drugs.

In routine clinical practice, the first choice in diagnosing a neuropathy would be to perform a routine neurological examination. If the results were normal, one would end the investigation. If the results were abnormal, or if controlled scientific research was being conducted on a potential, undefined, subclinical, or preclinical-type syndrome, one would then perform quantitative sensory testing and nerve or skin biopsies.

Other important health effects that should be examined include psychological or psychiatric changes or problems. There are well-known, useful neurobehavioral tests for neurotoxicity that are reliable (i.e., the results are replicable), valid in the sense that they detect established effects seen at higher concentrations as well as at low concentration exposure, and are specific for certain chemical classes and not for others. These neurobehavioral tests for neurotoxicity are the same tests as are used in neurological evaluations of other conditions. Neuropsychological tests are generally classified into domains of function. The domains most commonly applied include motor skills, general

intelligence and academic abilities, attention, executive function, verbal and language abilities, visuospatial skills, memory (anterograde, retrograde), and personality and affect.

In order to apply neuropsychological tests to clinical assessment, the technique used must allow the clinician first to document brain damage attributable to neurotoxicant exposure (from subtle to severe) and second, to feel comfortable attributing any observed deficits to neurotoxicant exposure rather than some other cause. It is important to explicitly rule out other potential causes of impairment such as age, education, smoking, alcohol use, developmental disorders, psychiatric disorders, neurological disorders, and motivational states in which persons consciously or unconsciously sabotage their own test performance.

A recent study of Oregon veterans investigated psychosocial, neuropsychological, and neurobehavioral elements to determine objective memory and attention impairment. The population-based study used questionnaires as well as clinical examinations to identify behavioral, psychosocial, and performance disorders. Results indicate that neurobehavioral tests can identify veterans with objective deficits in attention or memory and cognitive processes (Anger, 1996, Unpublished presentation). Whether these objective deficits result in clinical impairments has not yet been documented. In addition, although neurotoxic chemical exposure is one possible explanation for these outcomes, other possibilities exist.

Recommendations

The charge to the committee was to determine whether the Comprehensive Clinical Evaluation Program could adequately diagnose and treat possible health problems among service personnel who may have been exposed to low levels of nerve agents. The committee reviewed extensive clinical and research results regarding the effects of nerve agents. No evidence available to the committee conclusively indicated the existence of long-term health effects of low-level exposure to nerve agents. Because firm conclusions about these effects remain elusive, the committee reviewed information about the types of health effects that *might* exist as a result of exposure. Leading scientists presented information suggesting that the possible effects *might* include neurological problems such as peripheral sensory neuropathies and psychiatric problems such as alterations in mood, cognition, or behavior.

Recent reports suggesting a possible toxic synergistic effect following exposure to multiple agents known to influence cholinesterase activity will require extensive research to determine their significance (Haley and Kurt, 1997; Haley et al., 1997a,b; Lottie et al., 1993). The results of the research to date, however, did not appear to indicate any additional possible health effects should be considered by the committee other than those already identified.

The committee concluded that the CCEP continues to provide an appropriate screening approach to the diagnosis of disease. Most CCEP patients receive a diagnosis and 80% of participants receive more than one diagnosis. Although the types of primary diagnoses commonly seen in the CCEP involve a variety of conditions, 65% of all primary diagnoses fall into three diagnostic groups (1) psychological conditions; (2) musculoskeletal diseases; and (3) symptoms, signs, ill-defined conditions or a fourth group designated as "healthy." **However, in view of potential exposure to low levels of nerve agents, certain refinements in the CCEP would increase its value.** These

refinements are viewed as part of a natural evolution and improvement process and, therefore, need not be applied retrospectively. The committee does encourage rapid implementation in order to provide the benefits of an improved system to new enrollees.

The committee recommends improved documentation of the screening used during Phase I for patients with psychological conditions such as depression and posttraumatic stress disorder (PTSD). The DoD (DoD, 1996) reported that depression and PTSD account for a substantial percentage of those receiving a diagnosis of a psychological condition. In addition, if there are long-term health effects of nerve agent exposure, it is possible that these effects could be manifested as changes in mood or behavior. The committee will be conducting an in-depth examination of the adequacy of the CCEP as it relates to stress and psychiatric disorders at a later time; however, because of the increased importance of ensuring that all possibilities are thoroughly checked, better documentation in this area is encouraged. Primary physicians could use any of a number of self-report screening scales, but consistent use of the same scale across facilities would ensure consistent results.

The committee recommends improved documentation of neurological screening done during both Phase I and Phase II of the CCEP. Concern about nerve agent exposure as well as the number of nonspecific, undiagnosed illnesses among CCEP patients makes documentation of neurological screening extremely important. CCEP patients are referred to neuromuscular specialists if they have complaints of severe muscle weakness, fatigue, or myalgias lasting for at least 6 months that significantly interfere with activities of daily living. These patients are evaluated by board-certified neurologists who have subspecialty training in neuromuscular disease. Based on the description of the tests administered and examinations conducted, the committee finds that the CCEP is sufficient to ensure that no chronic, well-established neurological problem is being overlooked. The documentation of the use of these tests and procedures, however, could and should be improved. Such improvements would engender confidence that neurological examinations and treatments across facilities are comparable.

Given the importance of thorough neurological and psychiatric screening, **the committee recommends that Phase I primary physicians have ready access to a referral neurologist and a referral psychiatrist.** As mentioned earlier, patients are referred to neuromuscular specialists if they have complaints of severe muscle weakness, fatigue, or myalgias lasting for at least 6 months that significantly interfere with activities of daily living. Appropriate psychiatric referrals could include those with chronic depression that is treatment resistant, an unexplained, persistent complaint of memory problems, or significant impairment secondary to behavioral difficulties, such as not being able to maintain productive work due to behavioral abnormalities. While patients referred for Phase II consultations with a neurologist or psychiatrist are cared for adequately, it is sometimes difficult for the primary physician to determine

whether or not a referral is appropriate. In such instances, the physician tends to refer more frequently than not. It may be that, if the primary care physician had neurological and psychiatric consultations readily available, referral decisions could be made more easily and appropriately.

The committee recommends that physicians take more complete patient histories, particularly regarding personal and family histories, the onset of health problems, and occupational and environmental exposures. While there currently is grave concern about exposure to nerve agents during deployment in the Persian Gulf, other factors affect on psychological and neurological disorders. Patients can perform below expectations on neuropsychological tests for a number of reasons. In clinical assessments, therefore, it is important to rule out alternative causes of impairment. In addition, current and past exposures to occupational and environmental toxicants are important. Detailed histories are a valuable tool in identifying the etiology of a patient's problems.

The committee recommends that, to the extent possible, predeployment physical examinations given to members of the armed forces should be standardized among the services. The lack of uniform baseline information about service members makes diagnosis and treatment of postdeployment problems more difficult. To the extent that adequate baseline information is unavailable, physicians must rely on self-reporting. Adequate predeployment physical examinations, standardized across services, could prove an important tool for both clinical assessment and structured research.

The committee recommends that DoD increase the uniformity of CCEP forms and reporting procedures across sites. The CCEP system would benefit from increased consistency and the knowledge that each service is collecting and using the same information. Currently, each branch of service and each facility use different forms to complete examinations, tests, and referrals. Increasing the consistency of such forms and procedures would provide a more reliable picture of the care given to patients in the CCEP. As was stated in the 1996 report on the Health Consequences of Service During the Persian Gulf War, it is extremely important to create a uniform, continuous, and retrievable medical record. In addition, the 1996 report stated that the information should be collected according to standardized procedures and maintained in a computer-accessible format. (IOM, 1996b) The committee concurs with those findings.

For each patient, the physician should provide written evidence that all organ systems were evaluated. The CCEP primary care physicians examine patients, and, if there are problems requiring additional expertise, the patients are referred to specialists. This is standard medical practice used across the United States. It would be appropriate, however, for the CCEP primary care physicians to document that their evaluations covered all organ systems. The committee is not recommending the use of new or sophisticated testing mechanisms. It is reinforcing the importance of the components of the basic medical examination.

This increased documentation could be completed by noting the organ systems evaluated and whether each was normal or abnormal. For those listed as abnormal, additional information could be provided.

The committee strongly urges the DoD to offer group education and counseling to soldiers and their families concerned about exposure to toxic agents. Following the revelation by the DoD of possible exposure to nerve agents due to the destruction of the munitions dump at Khamisiyah, approximately 20,000 service personnel received a letter from the DoD stating that their units were in the vicinity during the demolition. Each recipient was encouraged to contact an 800 number if he or she was experiencing health problems believed to be a result of service in the Persian Gulf. Given this revelation, there may be a heightened sense of insecurity and concern among Persian Gulf veterans and their families about possible exposure to nerve agents. Risk communication is an important clinical activity. Family and group counseling can address heightened concerns about exposure as well as other issues. Such an approach provides an appropriate public health mechanism for imparting information and addressing concerns and should be made available to all Persian Gulf veterans.

Although it is beyond the scope of the charge to this committee to determine whether low-level exposure to nerve agents causes long-term health effects, the committee believes strongly that this is an important research area that ought to be pursued. Most of the literature regarding health effects of exposure to nerve agents (i.e., sarin and cyclosarin) addresses exposures high enough to cause clinically observable effects. These clinical effects are well documented and include miosis, blurred vision, nausea, vomiting, muscular twitching, weakness, convulsions, and death. Little known research has been conducted regarding the long-term health effects of low levels of exposure to these nerve agents. The application of findings from research on organophosphate pesticide exposure to the area of nerve agent exposure has limitations. However, even in such pesticide studies, long-term health effects have been documented only for acutely poisoned individuals—that is, persons with immediate clinical symptoms.

The committee emphasizes that the CCEP is *not* an appropriate vehicle for scientifically assessing questions about long-term health effects of low levels of exposure to nerve agents. *The CCEP is a clinical treatment program, not a research protocol.* It is important, therefore, not to attempt to use the findings of the CCEP to answer research questions. Those questions must be addressed through rigorous scientific research.

The committee notes that the CCEP could be useful in identifying promising directions for separate research studies. Examinations of the health effects—if any—of various wartime exposures have been hampered by poor information about the level of exposure and an inability to identify the individuals who may have been exposed. It is often difficult to retrospectively estimate exposure levels. However, information about where individuals were and when they were there could be combined with data regarding the presence of an exposure to

develop surrogate measures. These surrogate measures could then be linked to health information and used to examine potential associations between exposures and health effects.

Although data from the CCEP can not be used to *test* for associations, it can be combined with other information to help identify areas for future research. For example, the DoD identified approximately 20,000 service people belonging to units that were within a 50-kilometer radius of Khamisiyah at the time of the munitions demolition. Examining the health records of these people may yield insights into whether those who participated in the CCEP (or a similar program administered by the VA) have different illnesses or patterns of illnesses than do CCEP participants outside the 50-kilometer radius. More detailed discrimination of proximity to Khamisiyah (e.g., within 20 kilometers or within the units directly responsible for the munitions destruction) may provide additional information.

It is important, however, to understand the limitations of such comparisons. The results cannot be taken as research findings and generalized to the entire population of those deployed to the Persian Gulf. Active-duty military personnel participating in the DoD health registry may be either more or less healthy than other nonparticipants on active duty. CCEP comparisons on this self-selected group of patients should not be used to draw conclusions about the entire population of Persian Gulf veterans.

More broadly, the committee notes that information that helps to identify where individuals were in the Persian Gulf and when they were there will also facilitate research into potential service-related health problems. This information is currently needed to address the question of who might have been exposed to nerve agents and who could be part of the (unexposed) comparison groups necessary for epidemiological studies. Such information could also be used to more quickly and easily identify the exposed and unexposed groups that would be required to assess any future concerns regarding this or other exposures.

Generating geographical and temporal information for all 700,000 people who served in the Persian Gulf would be an immense endeavor. It would not be prudent to undertake such a task without first thoroughly understanding the effort required to complete it. It would, however, be appropriate to take steps now to identify and preserve records that could assist in the generation of such a database in the future. Records-based information is intrinsically superior to personal recollections, especially several years after the fact.

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Appendixes

Appendix A

Recommendations of the Initial CCEP Committee

Evaluation of the U.S. Department of Defense Persian Gulf Comprehensive Clinical Evaluation Program: Overall Assessment and Recommendations

Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program

Division of Health Promotion and Disease Prevention

INSTITUTE OF MEDICINE
Washington, D.C. 1996

1.) Overall Assessment of the CCEP Goals Procedures:

The Comprehensive Clinical Evaluation Program (CCEP) clinical protocol is a thorough, systematic approach to the diagnosis of a wide spectrum of diseases. A specific medical diagnosis or diagnoses can be reached for most patients by using the CCEP protocol. The Department of Defense (DoD) has made conscientious efforts to build consistency and quality assurance into this program at the many medical treatment facilities (MTFs) and regional medical centers (RMCs) across the country.

The committee is impressed with the quality of the design and the efficiency of the implementation of the clinical protocol, the considerable devotion of resources to this program, and the remarkable amount of work that has been accomplished in a year. The high professional standards, commitment, and diligence of the physicians involved in the CCEP at the RMCs were readily apparent at the three committee meetings. The committee commends the DoD for its efforts to provide high-quality medical care in the CCEP and the success that it has achieved to date in developing the infrastructure necessary to efficiently contact, schedule, refer, and track thousands of patients through the system.

Overall, the systematic, comprehensive set of clinical practice guidelines set forth in the CCEP are appropriate, and they have assisted physicians in the determination of specific diagnoses for thousands of patients across the country.

2.) General Recommendations for the Implementation of the CCEP:

2.1.) Referrals of Patients from Phase I to Phase II of the CCEP:

2.1.1.) Structure and Revise the CCEP Protocol and Logistics to Allow the Majority of Patients to Receive a Final Diagnosis by Phase I:

Currently, the majority of patients do not receive a final diagnosis until Phase II, yet some of these patients have straightforward medical problems. The Committee recommends that final diagnoses could be reached in Phase I if more diagnostic resources are made available. This major change would require the availability of substantial numbers of internists or family practitioners at MTFs to perform comprehensive evaluations. It would also require better, more consistent explanations to MTF physicians about the purposes and procedures of the CCEP. It would require regional medical center physicians to provide adequate quality assurance of MTF work-ups and timely feedback to MTF providers.

On January 17, 1995, the DoD adopted these suggestions by setting goals that about 80% of patients would receive a definitive diagnosis at an MTF level. For some patients, this change has required specialty consultations at the MTF, as well as advice from an RMC physician. These changes necessitated an enhanced quality control role by the RMC physician and prompt, appropriate feedback to the MTF physician.

2.1.2.) Curtail Diagnostic Work-ups in Patients Not Seriously Disabled with Minor Complaints:

Initially, patients who do not accept their initial diagnosis could request a continued evaluation all the way through Phase II. The Committee recommends that diagnostic work-ups in patients not seriously disabled but with minor complaints should be curtailed. Alternatively, if a physician has made a definitive diagnosis and appropriate treatment has been given, the evaluation would be concluded.

On January 17, 1995, the DoD implemented the suggestions that referral to Phase II be made on the basis of the clinical judgment of the primary care physician, and patients were no longer permitted to self-refer to an RMC.

2.1.3.) Require Additional Efforts to Provide More Care at the Primary Care Level:

The Committee encourages efforts to provide more care at the primary care level, because they will enhance the continuity of care and will foster the establishment of an ongoing therapeutic relationship.

2.1.4.) Continue Referral of Subgroups of Patients Whose Illnesses Are Difficult to Diagnose:

Patients whose illnesses are difficult to diagnose should continue to be referred to Phase II at an RMC. The decision to refer to Phase II should be based on the clinical judgment of the primary care physician, which, in turn, would be dependent on the clarity of the patient's diagnoses and the feasibility of the proposed treatment program at the MTF level. The DoD should continue its goal of enhanced accessibility of RMC physicians to allow regular consultations with MTF primary care physicians on patients with more complex diagnoses.

2.2.) Systematic Guidelines for Psychiatric Referrals and Adequacy of Psychiatric Resources:

2.2.1.) Develop Explicit Guidelines for the Identification of Phase I Patients Who Would Benefit from a Psychiatric Evaluation:

CCEP physicians have noted the need for standardized guidelines for screening, assessing, evaluating, and treating patients. Such Phase I guidelines should be developed to help ensure adequate psychiatric resources for both the initial evaluation and long-term follow-up care.

2.2.2.) Alert Primary Care Physicians About the High Prevalence of Psychiatric Disorders:

Two methods that have been proposed by RMC physicians to expedite the scheduling of psychiatric evaluations would be (1) the more frequent use of civilian psychiatrists and (2) consideration of using Ph.D.-level psychologists, as well as psychiatrists, when necessary.

3.) Specific Observations of and Recommendations for the Implementation of the CCEP:

3.1.) Analysis and Interpretation of the CCEP Results:

3.1.1.) Symptoms and Diagnoses in the CCEP Population:

3.1.1.1.) No Evidence Has Been Found that the DoD Has Been Trying To Avoid Reaching a Single Unifying Diagnosis:

The committee found no evidence that the DoD has been trying to avoid reaching a single "unifying" diagnosis when a plausible one was available. A "unifying" diagnosis is defined here as a single diagnosis that could explain most or all of a patient's symptoms.

3.1.1.2.) Signs and Symptoms in Many Patients Can Be Explained by Well Recognized Conditions:

One interpretation of the CCEP results is that the signs and symptoms in many patients can be explained by well-recognized conditions that are readily diagnosable and treatable. The committee concludes that this is a more likely interpretation than the interpretation that a high proportion of the CCEP patients are suffering from a unique, previously unknown "mystery disease."

3.1.1.3.) Provide More Detailed Information on Specific Diagnoses in Future Reports:

By providing more detailed information on specific diagnoses in its future reports, the DoD might help correct the impressions among the general public that exist about the high degree of prevalence of a "mystery disease" or a new, unique "Persian Gulf Syndrome."

3.1.1.4.) Investigate the Diagnosis in Patients with Disability Processing Actions:

Disability processing actions in the Services' Physical Disability Processing Systems have been completed for 246 of the 10,020 CCEP patients. The DoD has not provided any data about their diagnoses or their reasons for medical separation from the military. The committee recommends that the DoD investigate the diagnoses in this group of patients in future reports, as well as whether or not the disorders could have been caused or exacerbated by service in the Persian Gulf.

3.1.1.5.) Don't View CCEP Results as Estimates of the Prevalence of Disability Related to Persian Gulf Service:

Many other individuals who served in the Persian Gulf have left active service and, hence, are not eligible for the DoD's CCEP. Some of these veterans may have disabilities related or unrelated to their service in the Persian Gulf, and those with disabilities might be more likely to have left active service. For these reasons, the CCEP results should not be viewed as estimates of the prevalence of disability related to Persian Gulf service.

3.1.2.) Evidence of a New, Unique Persian Gulf Syndrome:

3.1.2.1.) There is a Lack of Clinical Evidence of a Unique Persian Gulf Syndrome:

The committee agrees with DoD that there is currently no clinical evidence in the CCEP of a previously unknown, serious illness among Persian Gulf veterans. If there were a new or unique illness or syndrome among Persian Gulf veterans that could cause serious impairment in a high proportion of veterans at risk, it would probably be detectable in the population of 10,020 CCEP patients. On the other hand, if an unknown illness were mild or affected only a small proportion of veterans at risk, it might not be detectable in a case series, no matter how large.

3.1.2.2.) Share the Entire CCEP Data Set with Qualified Researchers Outside of the DoD:

The committee encourages the DoD's plan to share the entire CCEP data set with qualified researchers outside of the DoD who might be able to undertake the kind of research with the methodological sophistication that the identification of a new syndrome would require.

3.1.3.) Potential Relationship of Illnesses in CCEP Patients to Service in the Persian Gulf:

3.1.3.1.) Discuss the Issue of Causality Explicitly and Unambiguously in its Future Reports:

Physicians involved with the development and the administration of the CCEP have, in various public presentations, acknowledged that some CCEP patients have developed illnesses that are directly related to their service in the Persian Gulf. The recent DoD report on 10,020 CCEP participants, however, only touches on this issue indirectly. The committee encourages the DoD to discuss the issue of causality explicitly and unambiguously in its future reports. Such a discussion might help to alleviate the current climate of confusion and mistrust that exists among some Persian Gulf veterans and the general public.

3.1.3.2.) Determine the Timing of the Onset of Disease:

The committee recommends that the DoD attempt to determine the timing of the onset of disease, especially for patients who have significant impairments. Review of military or civilian medical records that predate enrollment in the CCEP may provide contemporaneous documentation of the onset of symptoms in some patients, especially if the symptoms are serious. In addition, it is important to determine whether service in the Persian Gulf has contributed to the exacerbation of preexisting diseases in some CCEP patients.

3.1.4.) Comparison of the CCEP Population with Other Populations:

3.1.4.1.) Be Cautious About Comparison with Other Populations:

In its most recent report, the DoD compares the symptoms and diagnoses in the CCEP population with the symptoms and diagnoses in several community-based and clinically based populations. In the committee's view, interpretations based on comparisons with other populations should be made with great caution and only with the

explicit recognition of the limitations of the CCEP as a self-selected case series. The CCEP was not designed to answer epidemiological questions, such as how the frequencies of certain diagnoses compare between the CCEP population and a control population. Instead, it was designed as a medical evaluation and treatment program. Indeed, the research aims of the CCEP do not appear to be stated explicitly, nor does there appear to be a concrete epidemiological study plan. Without research hypotheses, it is not possible to judge whether any particular comparison group is appropriate. Each individual population should be described to prevent confusion.

3.1.4.2.) It's Difficult to Establish Causal Relationships by Relying on CCEP Data Alone:

It would be extremely difficult to establish causal relationships or to identify and characterize a new "Persian Gulf Syndrome" definitively by relying on data from the CCEP alone. The latitude permitted in the clinical examination program conflicts with the rigor necessary to answer an epidemiological question.

3.1.4.3.) Consider the CCEP Data to Have High Clinical Utility:

The CCEP data do have considerable clinical utility, and they could be used to address many important questions from a descriptive perspective. Many case series could be derived from these data. In addition, the results of the clinical exams could provide guidance in the selection of research questions and in the design of future epidemiological research. The CCEP findings could be used to generate epidemiological questions on other types of diseases that are much more frequent in the CCEP population, such as musculoskeletal diseases.

3.2.) Specific Medical Diagnosis:

3.2.1.) Psychiatric Conditions:

3.2.1.1.) Make Patients Aware of Psychiatric Conditions and Their Prevalence and Morbidity:

Patients need to understand that psychiatric conditions and disorders are real diseases that cause real symptoms and that diagnoses are made with objective criteria and are not merely "labels" applied because physical abnormalities were not found. The CCEP patients, as well as their primary care physicians, also need to understand the prevalence of and the concomitant morbidity that result from psychiatric disorders in the

general population (major depression, for example). Finally, the CCEP patients need to be aware that effective treatments that actually ameliorate symptoms exist for many of these disorders.

3.2.1.2.) Emphasize Effects and Diagnosis of Psychosocial Stressors:

In its future reports, the DoD is encouraged to emphasize that psychosocial stressors can produce physical and psychological effects that are as real and potentially devastating as physical, chemical, or biological stressors. The DoD should also emphasize that thorough efforts to diagnose psychiatric conditions in the CCEP population may lead to appropriate, successful treatments.

3.2.1.3.) Identify People with Risk of Developing Depression or Post-Traumatic Stress Disorder (PTSD):

The committee is particularly concerned about the CCEP patients who have developed or who are at risk of developing major depression or PTSD. These people need to be identified and provided with some form of preventive intervention.

3.2.1.4.) Improve Standardization of Psychiatric Evaluations:

The committee recommends that the DoD consider methods of improving the standardization of the psychiatric evaluations in the CCEP. The DoD should consider establishing detailed guidelines for the psychiatric evaluations and should attempt to obtain greater standardization of these evaluations among the various hospitals across the country. These guidelines could provide suggested procedures for the use of selected self-report instruments for the assessment of the most commonly diagnosed disorders, as well as procedures for more in-depth structured clinical interviews when indicated.

3.2.1.5.) Document and Investigate the Onset and Course of Symptoms and Psychosocial Stressors:

It would be especially important to document the onset and course of symptoms and to investigate their possible link with psychosocial stressors associated with mobilization and return home, as well as with service-related exposures in the Persian Gulf region. This assessment would require an additional set of questions to supplement the questionnaire currently used in Phase I of the CCEP. The thorough assessment of psychosocial stressors is essential information for treatment planning for patients with complex, chronic symptoms.

3.2.1.6.) Standardize Neuropsychological Evaluations:

Standardization of the neuropsychological evaluations is a related concern. The neuropsychological methods vary from pencil and paper testing at some sites to computer-administered testing at other sites. One method of achieving a better consensus is to convene a meeting attended by one psychiatrist and one neuropsychologist from each center to attempt to standardize their methods.

3.2.1.7.) Standardize Classification and Coding of Diseases:

In addition to the standardization of psychiatric evaluations in the CCEP, the classification and coding of these diseases should also be standardized.

3.2.1.8.) Document Headache Categories Differently:

The classification of different types of headaches into three separate categories may be consistent with ICD-9 coding rules, but the DoD should also report a special tabulation that combines all headaches into one group.

3.2.1.9.) Add Explicit Written Instruction on Medical Record-Keeping and Coding:

More explicit written instructions could be added to the CCEP guidelines to help prevent the most frequent problems found in the medical record-keeping and coding. Committee comments about inconsistencies are mainly aimed at the quality control necessary for accurate reporting of summary data rather than at the quality of the medical care itself.

3.2.1.10.) Expand Discussion of Psychological Stressors:

DoD should consider expanding discussion of the psychological stressors that were present during the Persian Gulf War.

3.2.1.11.) Utilize Results of On-Going Studies to Revise CCEP:

It is possible that the DoD will be able to use the results of on-going epidemiologic studies on psychiatric conditions to revise the CCEP, that is, to revise the standardized questionnaires or to add or delete targeted lab tests or specialty consultations. In addition, the CCEP clinicians may be able to utilize these results in the counseling and treatment of their

patients. These results may also be useful for the DoD in its planning to minimize the effects of psychosocial stressors in future deployments through the use of preventive medicine interventions.

3.2.2.) Musculoskeletal Conditions:

3.2.2.1.) Provide More Details of Diagnostic Categorization of Musculoskeletal Conditions:

The draft and final DoD reports on 10,020 CCEP patients do not provide adequate details for the IOM committee to make a thorough evaluation of the diagnostic categorization of musculoskeletal conditions. More explanation about the diagnostic aspects of these musculoskeletal conditions would be useful, for example, information on single-joint involvement versus multijoint conditions or articular versus non-articular conditions. In addition, details on disease severity and disease activity would be useful.

3.2.2.2.) Place More Emphasis on Musculoskeletal Conditions:

The DoD and the DVA should consider placing more emphasis on research on musculoskeletal conditions, since these are the most prevalent disorders among the CCEP populations.

3.2.3.) Signs, Symptoms and Ill-Defined Conditions:

3.2.3.1.) Clarify Types of Disorders Included in the ICD-9 Category:

The committee recommends that in future reports the DoD attempt to clarify the types of disorders that are included in the ICD-9 category of signs, symptoms, and ill-defined conditions (SSIDC). Individuals with these signs, symptoms, and ill-defined conditions should be evaluated in a rigorous manner, just as individuals with any other symptoms are evaluated.

3.2.4.) Infectious Diseases:

3.2.4.1.) Infectious Disease is Not a Frequent Cause of Serious Illness:

The IOM committee concludes that infectious diseases are not a frequent cause of serious illness in the CCEP population.

3.2.4.2.) Veterans are not Likely Afflicted With Some Previously Unknown Pathogen:

On the basis of the current evidence, it is unlikely that a significant proportion of Persian Gulf veterans are afflicted with some previously unknown pathogen that is evading the current diagnostic efforts.

3.2.5.) Chronic Fatigue Syndrome, Fibromyalgia, and Multiple Chemical Sensitivity:

3.2.5.1.) Estimating Prevalence of Chronic Fatigue Syndrome, Fibromyalgia, and Multiple Chemical Sensitivity is Difficult:

The IOM committee's review of the CCEP protocol suggests that data on chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivity (MCS) may have been collected by various diagnostic methods. For this reason, it is not possible to estimate the prevalence of these conditions from the CCEP data.

3.2.5.2.) Collect Data Using Established Diagnostic Criteria for CFS and FM:

In the clinical evaluations, data should be collected by using established diagnostic criteria for CFS and FM.

3.2.5.3.) Established Diagnostic Criteria Does Not Exist for MCS:

A widely accepted set of diagnostic criteria does not exist for MCS. Consequently, the medical evaluation in CCEP cannot be expected to diagnose the clinical syndrome of MCS.

3.2.5.4.) Include CFS, FM, and MCS in On-Going and Future Epidemiological Research Studies:

If more is to be learned about the relationship between these disorders (CFS, FM, and MCS) and Persian Gulf service, they should be included among the epidemiological research studies that are ongoing or planned for the future.

3.2.5.5.) Continue Thorough Workup to Diagnose Sleep Disturbances and Fatigue:

Because of the thorough, systematic work-up mandated in the CCEP, many disorders that could contribute to sleep disturbance and fatigue have been diagnosed. These diligent efforts to unmask occult medical problems that could substantially contribute to fatigue have been productive and should continue.

3.3.) Use of the CCEP Results for Education Improvements in the Medical Protocol, and Outcome Evaluations:

3.3.1.) Use of the CCEP Results for Education:

3.3.1.1.) Continue Public Release of Analysis Results of the CCEP on an On-Going, Periodic Basis:

The IOM committee encourages the DoD to continue to release its analysis of the results of the CCEP on an ongoing, periodic basis. Several audiences that would be interested in these results include active-duty members of the service, veterans, members of the U.S. Congress, the lay media, as well as military, DVA, and civilian medical and public health professionals. The CCEP medical findings would also be of interest to physicians in the DVA system and in the general community.

3.3.1.2.) Distribute CCEP Findings to all Primary Care Physicians at MTFs and RMCs:

The medical findings of the CCEP should be distributed promptly to all primary care physicians at the MTFs and RMCs. This would provide feedback on their diagnostic decision-making. Information on the frequencies of particular symptoms and their specific diagnoses made in the CCEP population could be useful, for instance, in developing a differential diagnosis for individual patients.

3.3.1.3.) Develop a More Concise Version of the DoD Report for Active-Duty Service Personnel and Veterans:

A more concise version of the DoD report on 10,020 patients, written in nontechnical language and with clearly stated conclusions, should be developed for a target audience of active-duty service personnel and veterans. If the DoD developed and distributed a fact sheet or newsletter aimed at Persian Gulf veterans, the information on the CCEP would be

more accurate and more comprehensive than most reports in the general news media. This would also provide an additional opportunity to notify the readers about the availability of the medical exam in the CCEP, the hotline number, and the eligibility criteria.

3.3.1.4.) Develop a More Comprehensive Document Describing Potential Exposures in More Detail:

The DoD should also consider developing for clinical use in the CCEP a more comprehensive document that describes the many potential exposures in more detail. Any document that is prepared, however, must make clear what is known and what is unknown about the relationship between these stressors and the physical or psychological consequences.

3.3.2.) Use of the CCEP Results to Improve the Medical Protocol:

3.3.2.1.) Use CCEP Examination Results to Improve Standardization Practices:

The DoD now has results on the examinations of more than 10,000 CCEP patients, which could be used to improve the standardized questionnaires, lab tests, and specialty consultations.

3.3.2.2.) Refine Questions Related to Potential Psychological Stressors:

More refined questions related to potential psychological stressors could be added systematically to the Phase I medical history. The CCEP physicians might find this information useful in diagnosing and counseling their patients. In addition, it may be possible to identify patients who are at increased risk of psychological problems on the basis of their experiences in the war. Perhaps explicit questions on death exposure and other known risk factors could be added to the Phase I questionnaire.

3.3.2.3.) Determine if Lab Tests or Specialty Consultations Should be Added to Phase I:

The CCEP results should be analyzed to determine whether there are lab tests or specialty consultations that should be added systematically to Phase I to increase its diagnostic yield. Diseases that are diagnosed relatively frequently in Phase II may often be overlooked in Phase I. If

such diseases could be identified, perhaps appropriate screening instruments could be added to Phase I.

3.3.2.4.) Compare and Coordinate Methods and Clinical Results of the CCEP and UCAP:

The DVA uses a protocol similar to that used in the CCEP called the Uniform Case Assessment Protocol (UCAP). The methods and clinical results of the CCEP and UCAP should be compared to coordinate and improve the two programs.

3.3.3.) Use of the CCEP Results for Patient Outcome:

3.3.3.1.) Perform Targeted Patient Evaluations:

On the basis of more than 10,000 patient evaluations to date, RMC physicians could begin to perform a series of targeted patient evaluations. The most common diseases in the CCEP could be identified, and suggested approaches to patient treatment could be developed. Consensus guidelines for the treatment and counseling of CCEP patients who have the most common disorders could be useful for primary care physicians.

3.3.3.2.) Communicate Successful Treatment Methods Between RMCs:

If one RMC has had a lot of experience with a particular disease category and some measure of success in its treatment, the DoD could ensure that a description of their successful methods is communicated to the other MTFs and RMCs across the country.

3.3.3.3.) Review Disorders Among CCEP Patients who Have Applied for Disability Payments of for Medical Discharge from the Service:

The DoD could perform a review of the types and severities of the disorders among CCEP patients who have applied for disability payments or for medical discharge from the service. In addition, the final disposition of these cases could be evaluated, including the potential relationship between particular diseases and Persian Gulf service. The DoD could use the results of these disability determinations to predict which diseases are likely to be associated with the most impairment among CCEP patients in the future. The DoD could also use these results to develop rehabilitation and early intervention methods for impaired Persian Gulf veterans, such as the

Specialized Care Centers (SCC). Another reason to analyze these disability claims would be to investigate possible preexisting risk factors for the development of the impairment. If such risk factors are identifiable, then targeted preventive medicine interventions could be planned for individuals participating in future overseas deployments.

3.3.4.) Specialized Care Center (SCC):

3.3.4.1.) The DoD has Made Serious Efforts to Develop an SCC Program that has Ambitious Goals:

The IOM committee concludes that the DoD has made serious efforts to develop an SCC program with ambitious goals for a select group of seriously impaired military personnel. The committee's review should be considered preliminary, however, because it is based on one visit and it is still early in the development of the program.

3.3.4.2.) Provide Multidisciplinary Treatment Modalities:

The SCC currently performs a thorough reevaluation of each patient's medical problems. SCC physicians should consider limiting the diagnostic role that they play to focusing on the incoming patients who have been very difficult to diagnose at the RMC level. Instead, the SCC should focus on providing multidisciplinary treatment modalities that are not readily available at the RMC level.

3.3.4.3.) Need for Individualized Follow-Up and Therapeutic Regimens:

The need for individualized follow-up is crucial for the types of difficult patients who are likely to be treated at the SCC. Medical staff at the SCC will need to know whether a particular therapeutic plan is feasible at the patient's nearest MTF and whether long-term follow-up care can be performed. The primary care physician at the MTF needs to encourage continuous patient compliance with the carefully designed, individualized therapeutic regimens.

3.3.4.4.) Develop Objective Measure of Functional Status for Follow-Up Evaluation:

The SCC physicians should develop a set of relatively objective measures of functional status for the follow-up evaluation. These could include (1) appropriate utilization of medical care, (2) appropriate use of medications or other methods to cope with symptoms, (3) general

level of activities of daily living, (4) employment status, and (5) status of interpersonal relationships.

3.3.4.5.) Evaluate the SCC Program Itself:

The SCC program itself needs an evaluation component after several of its graduates have returned for their 6-month reevaluations. Several issues will need to be evaluated in light of the successes and barriers that the program has experienced, including eligibility criteria for patients; roles of the SCC in a diagnostic reevaluation of patients; successful continuity of care of patients, with shared responsibility by the SCC and MTFs; and the unique need for the SCC, beyond the usual standard of a tertiary care medical center.

3.3.4.6.) DoD Has Taken a Serious Approach to the Treatment and Rehabilitation of these Patients in the SCC:

The committee believes that the DoD has taken a serious approach to the treatment and rehabilitation of these impaired patients who have treatable, chronic diseases.

3.3.4.7.) Investigate Costs and Benefits of the SCC Program:

Because this program is very labor intensive, it is probably very expensive on a per-patient basis. At the same time, the potential benefits for each patient could be high, if successful rehabilitation of serious, long-term impairment can be achieved. Subsequent evaluations of the SCC program should investigate its costs and benefits, if possible.

3.3.4.8.) Identify the Most Effective Elements of the SCC Program:

If the SCC program is successful in improving the health and functional status of its patients, perhaps the elements that are most effective in enabling the patients to cope with their symptoms could be identified. Perhaps some of these elements could be disseminated and integrated into existing MTF programs that are close to where CCEP patients live and work.

3.4.) Research Relevant to the CCEP:

3.4.1.) Epidemiological Research Relevant to the CCEP:

3.4.1.1.) Utilize On-Going Epidemiological Studies for Revising or Improving the CCEP:

The results of on-going epidemiological studies may be useful for making revisions or improvements in the CCEP medical protocol itself, for example, to revise the standardized questionnaires or to add or delete targeted lab tests. The study results may also be useful in the counseling and treatment of CCEP patients.

3.4.1.2.) Acknowledge the Serious Limitations of the CCEP Data for Epidemiological Purposes:

Data from individuals in the CCEP are also being used in some of these epidemiological studies. In these studies, the serious limitations of the CCEP data for epidemiological purposes that were previously identified must be kept in mind.

3.4.2.) Exposure Assessment Research Relevant to the CCEP:

3.4.2.1.) Investigate Experiences of Individuals in UICs with Higher Rates of CCEP Participation:

The IOM committee encourages DoD to perform further investigations on the war and postwar experiences of individuals in the Unit of Assignment Codes (UICs) with higher rates of CCEP participation.

3.4.2.2.) Investigate Exposures Restricted to Particular Locations or Special Occupational Groups:

The committee encourages the DoD to investigate exposures that were restricted to particular locations or special occupational groups, such as troops who had direct combat exposure. The types of symptoms and diseases in CCEP participants in these special groups and UICs could be analyzed and contrasted with the symptoms and diagnoses of CCEP participants in other units.

COMMITTEE ON THE DOD PERSIAN GULF SYNDROME COMPREHENSIVE CLINICAL EVALUATION PROGRAM

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Appendix B

Outline of the CCEP Medical Protocol

Form Requirements

At the MTF level, the CCEP record should include all CCEP forms and relevant medical data to the program.

Blank forms included with this guide supersede previous editions of these forms and are intended to be used with the new CCEP.

All individual forms will be complete and legible.

Forms forwarded to NMIMC and maintained in the participant record shall be in the following order:

Phase I completed:

MTF Phase I Diagnosis Form
Patient Questionnaire
Provider-Administered Symptom Questionnaire
Information Release Form
Declination/Completion Form

Phase II completed:

RMC Phase II Diagnosis Form
Declination/Completion Form

Medical Protocols

The CCEP is based upon a thorough clinical evaluation which emphasizes comprehensive and continuous primary care. The local MTF primary care provider maintains responsibility for patient evaluation and care throughout the CCEP process.

Medical Treatment Facility (Phase I):

Phase I will consist of a comprehensive history and medical evaluation with completion of Phase I questionnaires and related forms. The examination, both in content and quality, should parallel an in-patient admission work-up. The Phase I examination will include a complete medical history including: family, occupation, social (including tobacco, alcohol, and drug use), exposure to possible toxic agents, psychosocial condition and review of symptoms. The provider will specifically inquire about the symptoms listed on the CCEP Provider-Administered Patient Questionnaire. A comprehensive medical evaluation, with focused attention to the patients symptoms and health concerns, should be conducted.

Individuals who, after completing MTF Phase I evaluations do not have a clearly defined diagnosis which explains their symptoms should be reviewed by the CCEP designated physician for further evaluation and consultations needed and/or for referral to the RMC.

Phase II Level Evaluations are performed only after complete clinically indicated evaluations (including appropriate specialty consultations) are conducted at the MTF and the RMC.

Phase I Laboratory Tests

CBC
U/A
SMA-12

Regional Medical Center (Phase II):

Phase II evaluations consist of the following laboratory tests, consultations and as necessary, symptom-specific examinations. J Elements of the Phase II evaluation may be accomplished by the local MTF as needed in the comprehensive evaluation of the Phase I patient in order to obtain a definitive diagnosis.

Phase II Laboratory Tests

CBC
Sedimentation rate (ESR)
C-Reactive protein
Rheumatoid factor
ANA
Liver function
CPK
Urinalysis
TB skin test (PPD) with controls
Chest X-ray
Hepatitis serology
HIV testing
VDRL
B12 and folate
Thyroid function tests

Phase II Consults

(if not accomplished at MTF level)
Dental: Dental only if participant's annual screening not done
Infectious disease
Psychiatry: With physician-administered instruments:
Structured Clinical Interview for DSMIII-Rcm (SCID) (delete modules for mania and psychosis)
Clinician-Administered PTSD Scale (CAPS)

Neuropsychological Testing: Only as indicated by psychiatry consult

Symptom-Specific Examinations

The RMC CCEP Physician ensures that Phase II patients with the following undiagnosed symptoms receive the tests and consultations listed below.

Diarrhea
GI consult
Stool for O and P
Stool Leukocytes
Stool culture
Stool volume
Colonscopy with biopsies
EGD with biopsies and aspiration

Abdominal
GI consult
EGD with biopsy/ aspiration
Colonscopy with biopsy
Abdominal ultrasound
UGI series with small bowel FT
Abdominal CT scan

Headache
MRI—head
LP (glucose protein, cell count, VDRL, oligoclonal myelin, basic protein, pressure)
Neuro consult

Muscle Aches/Numbness
EMG/NCV

Chronic Fatigue
Polysomnography and MSLT

Chronic Cough/SOB
Pulmonary consult
Pulmonary function
Tests with exercise and ABG
Methacholine challenge
If PFTs are normal, consider bronchoscopy with biopsy/lavage

Memory Loss
(Only if verified by psych evaluation)
MRI—head
Lumbar puncture
Neuro consult
Neuro psych testing

Chest Pain/Palpitations
ECG
Exercise stress test
Holter monitor

Reproductive Concerns
Urology consult
GYN consult

Vertigo/Tinnitus
Audiogram
ENG
BAER

Skin Rash
Dermatology consult
Consider biopsy

Appendix C

Workshop on the Adequacy of the CCEP for Evaluating Individuals Potentially Exposed to Nerve Agents: Agenda and Speakers List

NATIONAL ACADEMY OF SCIENCES INSTITUTE OF MEDICINE
December 3, 1996
Foundry Building FO-2004, Georgetown

Agenda

10:00–10:15	Welcome/Purpose and Conduct of the Workshop Dr. Dan Blazer, Chair, Committee on the Evaluation of the DoD Comprehensive Clinical Evaluation Program for Persian Gulf Veterans
10:15–12:00	Workshop Session I—Issues regarding the CCEP Dr. Raymond Chung, *Origins/Background* Dr. Charles Engel, *Mental Health* Dr. Andrew Dutka, *Neurologic Conditions* Dr. Timothy Cooper, *Pain* Dr. Anthony Amato, *Neuromuscular Symptoms* Dr. Kurt Kroenke, *Diagnostic Approach/Generalized Symptoms*
12:00–1:00	Lunch in meeting room
1:00–2:45	Workshop Session II—Issues regarding organophosphates, anticholinesterases and nerve agents Dr. Peter Spencer, *Neurotoxicology of organophosphates* Dr. Robert MacPhail, *Behavioral toxicology of organophosphates and pyridostigmine*

	Dr. Robert Gum, *Possible health effects in humans from low level exposure to nerve agents* Dr. Bhupendra P. Doctor, *Endogenous detoxification of sarin*
2:45–3:00	Break
3:00–4:45	Workshop Session III—Issues regarding neurological testing protocols Neurophysiological testing Dr. Eva Feldman Dr. David Cornblath Neurobehavioral and neurocognitive testing Dr. Kent Anger Dr. Roberta White
4:45–5:00	Break
5:00–6:30	Workshop Session IV—Moderated Discussion Dr. Dan Blazer, *Moderator* Dr. Richard Johnson Dr. Arthur Asbury Dr. David Janowsky
6:30	Workshop adjourns

SPEAKERS LIST

December 3, 1996
Foundry Building, Georgetown

Anthony A. Amato, M.D.
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Department of Neurology and Medicine

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Boston

Appendix D

DoD Memorandum for Persian Gulf War Veterans Concerning Khamisiyah, Iraq

DEPUTY SECRETARY OF DEFENSE

1010 DEFENSE PENTAGON
WASHINGTON, DC 20301-1010

October 1996

MEMORANDUM FOR PERSIAN GULF WAR VETERANS CONCERNING KHAMISIYAH, IRAQ

The Department of Defense is continuing its wide-ranging investigation of incidents that might be related to Persian Gulf veterans' illnesses. We are asking for your help in providing us with important information.

Evidence from an ongoing investigation indicates that chemical weapons were present when U.S. forces destroyed a series of ammunition storage bunkers and crated munitions in an open pit area at a complex called ''Khamisiyah'' or "Tal al-Lahm," about 15 miles southeast of "An Nasiriyah" in southern Iraq. Our records show that your unit participated in the demolition operations at Khamisiyah in March 1991.

To our knowledge, service members at that time did not report the symptoms associated with acute exposure to chemical agents (nerve gas), but our search for information continues. Since you may have been part of the demolition operations, we need to hear from you, not only about your experience at or near the site but also any health problems you think may be a result of your service during Operation Desert Storm/Operation Desert Shield.

We urge you to call our PERSIAN GULF INCIDENT HOTLINE at 1-800-472-6719. When you call please indicate you were a member of the Khamisiyah demolition team. The person answering the telephone will ask you a few simple questions and then, if you desire, refer you to an appropriate medical facility for medical evaluation and care. We want to be sure you receive any health care you may need for health problems related to your service in the Gulf War.

Be assured, the Departments of Defense and Veterans Affairs are working together to bring all necessary resources to bear on this issue. But we can not do it alone. To understand the events at Khamisiyah and to address the concerns of our Gulf War veterans, we need your help in this effort.

We are indebted to each one of you for your service to our country during the Persian Gulf War.

John P. White

Enclosure: Frequently Asked Questions and Answers

Frequently Asked Questions and Answers About Khamisiyah

Here are the answers to several frequently asked questions relating to the events at Khamisiyah.

Q: What kinds of weapons were destroyed by U.S. forces at Khamisiyah?

A: Khamisiyah was a large Iraqi ammunition storage site. Of the approximately 100 bunkers destroyed in March 1991, one has been assessed by UNSCOM (United Nations Special Commission) to have held 122mm rockets containing chemical agents (the nerve agents sarin and cyclosarin). In addition, rockets containing these nerve agents were found by UNSCOM inspectors in an open pit near the bunker complex, where U.S. forces also conducted demolition operations in March, 1991.

Q: What are the effects of these chemical weapons?

A: As you may recall from your training, chemical weapons create serious immediate symptoms (blurred vision, tightness in the chest, runny nose, dizziness) and, if immediate treatment is not provided, can incapacitate or kill troops on the battlefield. While research continues, the best current medical evidence indicates you should not experience long-term health problems from low level exposure to chemical nerve agents.

Q: Were any such symptoms experienced by our troops during the Gulf War?

A: To our knowledge, service members neither died or reported such immediate symptoms in connection with Khamisiyah. Soldiers reported possible chemical events during the war, but we have been unable to confirm any nerve agent exposure from these reports.

Q: What are the long-term health effects of non-lethal exposure to nerve agent?

A: Although they are limited in number, studies of human exposure to nerve agent suggest that no long-term health effects from low level, short-term exposure to nerve agent are likely, even when doses are large enough to produce some immediate symptoms. We are stepping up the research directed toward finding a more definitive answer to this question.

Q: If I, as a Gulf War veteran, experienced no symptoms at the time and studies indicate there are no long-term health effects, why am I receiving this letter and being asked to call the hotlines?

A: First, we are asking your help in our understanding of the events surrounding Khamisiyah. Second, we want to be sure you receive any health care you may need for health problems related to your service in the Gulf War.

Appendix E

Persian Gulf War-Related Events: Timeline

Date			Significant Event
1990	August	2	Iraq invades Kuwait
1990	August	8	U.S. Air Force arrives in Saudi Arabia
1990	August	9	U.S. ground forces arrive in Saudi Arabia
1990	November	29	UN Security Council authorizes use of force to eject Iraq from Kuwait
1991	January	12	Congress authorizes use of force to eject Iraq from Kuwait
1991	January	16	Operation Desert Storm commences as U.S. warplanes attack military targets in Iraq and Kuwait
1991	January	17	First hostile fire
1991	January	20	First oil well fires started in Kuwait
1991	January	27	Coalition forces declare air supremacy
1991	February	19	Majority of oil well fires ignited
1991	February	24	Ground war begins
1991	February	25	SCUD attack in Dhahran killing U.S. troops
1991	February	28	Cease-fire takes effect and offensive operations end
1991	March	10	U.S. troops destroy munitions dump at Khamisiyah
1991	June	13	Last U.S. ground troops return to the United States
1992	August		Expert Panel on Petroleum Toxicity established
1993	July		Office of Technology Assessment Workshop on Persian Gulf Health held
1993	October		Start of IOM Committee to Review the Health Consequences of Service During the Persian Gulf War
1993	December		Defense Science Board established
1994	January		Persian Gulf Veterans Coordinating Board established
1994	April		National Institutes of Health Technology Assessment Workshop Panel held
1994	May		Independent Council Harrison Spencer (dean, Tulane University School of Public Health) appointed
1994	June		IOM Committee to Review DoD's Comprehensive Clinical Evaluation Program established
1994	December	2	IOM Committee on the Comprehensive Clinical Evaluation Program's first report submitted to DoD
1995	March		Senior-Level Oversight Panel, Persian Gulf Investigation Team, and Declassification Program established
1995	March		Task Force on Analysis and Declassification of Intelligence Records established
1995	May	26	Presidential Advisory Committee of Gulf War Veteran's Illnesses established
1995	August	7	IOM Committee on the Comprehensive Clinical Evaluation Program's second report submitted to DoD

Date			Significant Event
1996	January		IOM Committee on the Comprehensive Clinical Evaluation Program's final report submitted to DoD
1996	March		DoD releases report, "The Possible Role of Vaccine Adjuvants in Persian Gulf War Veterans Illness"
1996	March	11	Congressional hearings held on "Status of Efforts to Identify Persian Gulf War Syndrome Part I"
1996	March	28	Congressional hearings held on "Status of Efforts to Identify Persian Gulf War Syndrome Part II"
1996	June	21	DoD announces that suspected chemical weapons might have been at the Khamisiyah Ammunition Storage Depot (300–400 U.S. troop potentially exposed to nerve agents)
1996	June	25	Congressional hearings held on "Status of Efforts to Identify Persian Gulf War Syndrome Part III"
1996	August	2	CIA releases report on Intelligence Related to Gulf War Illness
1996	August	4	DoD releases report on "Coalition Chemical Detectons and Health of Coalition Troops in Dectection Area"
1996	August	8	DoD releases "Report on Possible Effects of Oganophosphate 'Low-Level' Nerve Agent Exposure"
1996	September	4	DoD releases CCEP Database for Independent Scientific Investigation
1996	September	19	Congressional hearings held on "Status of Efforts to Identify Persian Gulf War Syndrome Part IV"
1996	September	19	DoD revises estimate of number of troops potentially exposed to nerve agents to 5,000
1996	October	2	DoD revises estimate of number of troops potentially exposed to nerve agents to 15,000
1996	October	22	DoD revises estimate of number of troops potentially exposed to nerve agents to 21,000
1996	November		Special Assistant to Gulf War Veterans Illnesses appointed
1996	November		Special Assistant to the President for Gulf War Veterans Illnesses appointed
1996	December		Second IOM Committee to Review DoD's Comprehensive Clinical Evaluation Program established
1996	December	10	Congressional Hearings held on "Status of Efforts to Identify Persian Gulf War Syndrome Part V"
1996	December	31	Presidential Advisory Committee submits its final report
1997	January	9	Senate hearings held on "Persian Gulf War Illnesses"
1997	January	21	Congressional hearings held on "Status of Efforts to Identify Persian Gulf War Syndrome Part VI"