Following the Gulf War, some veterans of that conflict began reporting a variety of health conditions and other symptoms, some of which remain unexplained. The Department of Defense (DoD), as part of its effort to inquire into possible causes of these illnesses, has commissioned various studies of the scientific literature about potential or contributing causes of illnesses in Gulf War veterans. 1 This document represents one such study. It focuses on infectious diseases with the goal of presenting current medical knowledge regarding these diseases, irrespective of the specific issues surrounding the Gulf War. When appropriate, it interprets whether a particular infectious disease or related condition is likely to explain symptoms experienced by those who served in the Gulf War.

Infectious diseases have been extensively studied and their identification, diagnosis, and treatment are generally well understood. Therefore, this study does not consider all infectious diseases. Rather, it focuses on known or plausible ones—those that were actually diagnosed in people who served in the Gulf War or that are known either to exist in the Persian Gulf area or to produce symptoms similar to those experienced by Gulf War veterans. A complete review of the scientific literature, even as it pertains to the discussed infectious diseases, is beyond the scope of this volume.

An early study by the Centers for Disease Control and Prevention showed three types of symptoms as being about three times more prevalent among those who had served in the Gulf War: chronic fatigue, joint and muscle pain, and neurocognitive symptoms. However, the symptoms described were not unique to service in the Persian Gulf War.

1Throughout this report the term “Gulf War illnesses” is intended to refer generally to symptoms experienced by veterans who served in the Gulf War, irrespective of whether those symptoms are explained or unexplained.
After the review of the scientific literature about infectious diseases, we make the following observations:

- Of the known infectious diseases (i.e., known to have infected veterans or known to be present in the area of the conflict), none seems likely to cause the undiagnosed illnesses in Gulf War veterans.

- That said, the patterns of infectious diseases have some similarities to some cases of undiagnosed illnesses among Gulf War veterans. Therefore, we cannot entirely rule out some unknown infectious disease as a possible cause of illness for some individuals.

- At present, most commonly recognized infectious diseases have been ruled out as a major factor among ill Gulf War veterans. One theory that continues to merit investigation concerns the role of *Mycoplasma* infection as a cause. More testing is currently under way to evaluate the relationship between *Mycoplasma* infection and illness in Gulf War veterans.

**INFECTIOUS DISEASES**

A case can be made both for and against infectious diseases as a cause of the illnesses among Gulf War veterans. The argument for an infectious cause includes the belief that symptoms reported by Gulf War veterans represent an epidemic among a group of people with a common exposure, in this case service in the Middle East during the war. History bolsters this interpretation. Typically, some time passes before a cause is identified for an observed set of symptoms. AIDS is a case in point. In that case, several years passed after the observation of a set of symptoms before a virus and diagnostic test were identified. Furthermore, some of the infectious diseases diagnosed among Gulf War participants, most notably *Leishmania*, produce some symptoms similar to those described by Gulf War veterans.

However, some factors weigh in against infectious disease as a cause. For example, the veterans do not have a common, measurable sign, such as a fever, abnormal laboratory test, or anatomic lesion (e.g., sores, rash). Although some veterans present anatomic lesions, the lack of a consistent set of signs and symptoms makes it difficult to conclude that a single infectious disease could be the cause.

**INFECTIOUS DISEASES AMONG GULF WAR VETERANS**

During the earliest stages of deployment when the weather was extremely hot, acute diarrheal disease was the major infectious disease problem (Hyams et al., 1995). The most commonly identified enteropathogens were multidrug-resistant
enterotoxigenic *Escherichia coli* (ETEC) and *Shigella sonnei*. There were no laboratory-confirmed cases of cholera, typhoid fever, amoebic dysentery, or giardiasis. Viral gastroenteritis became a problem after the weather became cooler in December 1990. Acute upper respiratory infections were also prevalent, especially during periods of crowded travel and billeting (Hyams et al., 1995).

In this deployment, there were no documented cases of sandfly fever, and outbreaks of febrile illness consistent with insect-borne infections were not reported (Richards et al., 1993). There was one confirmed case of West Nile fever, seven cases of malaria among U.S. troops who went into southern Iraq, and three cases of Q fever. Brucellosis was not diagnosed among western troops, and viral hepatitis was an infrequent problem. One chronic infectious disease that has been linked to service in the Middle East was viscerotropic leishmaniasis. This sandfly-transmitted infection has been diagnosed in 12 U.S. veterans but not in other coalition personnel (Magill et al., 1993). Viscerotropic leishmaniasis is a comparatively mild form of systemic leishmanial infection caused by *Leishmania tropica*, a eukaryotic parasite that typically produces cutaneous disease. In addition, 20 U.S. Gulf War veterans have been diagnosed with cutaneous leishmaniasis caused by *L. major* infection (Kreutzer et al., 1993).

**OTHER DISEASES**

Several diseases known to exist in and around the Kuwaiti Theater of Operations were not identified in any of the veterans. These include sandfly fever (phlebotomus fever), dengue fever, typhus, and brucellosis. Other infections also were considered as possibly related, including mycoplasmosis, tuberculosis, anthrax, and botulism. The latter two were considered because they are biological warfare agents.

**LEISHMANIA**

*Leishmania* is a vector-borne parasite transmitted in Southwest Asia by the sandfly, *Phlebotomus papatasi*. It is of interest to the study of the illnesses among Gulf War veterans because it exists in the Kuwaiti Theater of Operations, causes some of the same symptoms observed in the illnesses among Gulf War veterans, and has been found in some of the veterans. Although different species of *Leishmania* look the same under a microscope, they have different effects on their hosts. Two types of syndromes—cutaneous and visceral leishmaniasis—are of particular interest because they exist in the area, and both have been diagnosed in veterans. The cutaneous form appears two to eight weeks following infection, although some cases have been reported as long as a year later. It manifests itself as ulcers that form at the site of the bite. Twenty
cases of this type of leishmaniasis were diagnosed. Visceral leishmaniasis involves multiple organs in the body, can be quite virulent, and can result in death. The type experienced by the Gulf War veterans appears to be a milder form, termed viscerotropic leishmaniasis, and 12 cases have been diagnosed.

**BIOLOGICAL WARFARE AGENTS**

Coalition troops feared, with some justification, that Iraq might use biological weapons against them. The two most likely candidates were anthrax and botulinum toxin. Fortunately, both are well understood and diagnosis, treatment, and prevention strategies exist for each. Both agents have severe, life-threatening symptoms, and neither is known to have a chronic state. Thus, if these agents were used against coalition troops, we would have expected multiple individuals to become symptomatic shortly after exposure. Low-level exposures do not appear likely.

**MYCOPLASMA**

*Mycoplasmas* are the smallest free-living microorganisms, and cause disease in plants, animals, and humans. One strain has been reported in a number of veterans who have the symptoms of the Gulf War illnesses. A technique called nucleoprotein gene tracking has been developed to detect the bacteria in patients, and a rigorous study has been designed and is under way to validate this technique and compare it to a more established technique, namely, the polymerase chain reaction. Meanwhile, several sources have reported high rates of *Mycoplasma* in ill Gulf War veterans using genetic techniques. Tests assessing antibody production against *Mycoplasma* have not produced these high rates, but many people may not generate antibodies to this organism if infected, reducing the sensitivity of antibody techniques for detecting *Mycoplasma* infection.

**UNIDENTIFIED INFECTIONS**

A final possibility is that a previously unidentified infectious disease is causing illnesses among Gulf War veterans. There is no positive evidence to suggest that this is the case; however, it cannot be ruled out. Some of the routine tools for identifying differences between those with and without illnesses among Gulf War veterans are not available because too much time has passed. Other techniques, for example, screening pre- and postwar blood samples, have been tried on available samples but to date have yielded no positive results. Other sophisticated techniques, such as DNA or genetic analysis, are possible.