

GULF WAR RISK FACTOR REPORT REPRINT

Infectious Diseases

The following article originally appeared in the January 2001 issue of the Gulf War Review newsletter. For information about the newsletter, contact Mr. Donald J. Rosenblum, Deputy Director, Environmental Agents Service (131), VA Central Office, 810 Vermont Avenue, N.W., Washington, DC 20420, telephone: 202-273-8580.

Gulf War Veterans and Infectious Diseases

This is one of a series of articles about various environmental hazards or risks encountered by military personnel deployed to Gulf War theater of operation. Previous articles have focused on chemical and biological warfare agents, pesticides, depleted uranium, and pyridostigmine bromide.

Based on high rates of infectious disease illness among Allied troops sent to the Persian Gulf during World War II, Gulf war troops were expected to be at increased risk of sand fly fever, malaria, diarrheal disease, viral hepatitis, and cutaneous leishmaniasis. To monitor for these diseases, the U.S. military established a state-of-the-art diagnostic laboratory in Saudi Arabia, which was involved in the collection of large amounts of surveillance (watching and monitoring) data during Operations Desert Shield and Desert Storm.

In the earliest stages of deployment when the weather was extremely hot, outbreaks of common traveler's diarrhea were frequent. However, there were no laboratory-confirmed cases of more severe diseases, including cholera, typhoid fever, amoebic dysentery, or giardiasis. Acute vomiting became a problem after the weather became cooler in late 1990. Acute upper respiratory illnesses (for example, colds) also were common during periods of crowding.

Despite active surveillance, there was no documented case of sandfly fever or outbreaks of illness consistent with insect-transmitted infections during the war. There was one confirmed case of West Nile fever (a common infection in this region), seven cases of malaria among U.S. troops who went into southern Iraq, three possible cases of Q fever, and one death due to meningococcal meningitis. Brucellosis was not diagnosed among U.S. troops, and viral hepatitis was a rare problem.

A combination of factors was probably responsible for very low rates of serious infectious diseases during the Gulf War deployment. For one, rapid medical care and effective treatment were available for infectious diseases. In addition, extensive preventive medicine efforts -- vaccinations, immune globulin for hepatitis A prevention, use of insecticides and repellents, camp sanitation measures, and inspection of food and

water supplies -- reduced the risk of infectious diseases. Lastly, restricted contact with local populations lowered infectious disease transmission.

Two unplanned factors also may have played a major role in preventing infectious disease problems: the time of the year when most troops were deployed (the cooler winter months) and the location of deployment (the barren desert). Cold weather reduced insect activity at the height of the buildup in January 1991, and the risk of disease transmission was lowered by deploying most troops away from oases and rivers where insects and animals that host infectious diseases are more abundant.

Leishmaniasis

Since the Gulf War, one chronic infectious disease -- viscerotropic leishmaniasis - has been definitely linked to service in the Persian Gulf. This sandfly-transmitted infection has been diagnosed in just 12 U.S. veterans, but not in any of the other coalition troops. Viscerotropic leishmaniasis is a milder form of systemic leishmanial infection caused by a one-celled parasite *Leishmania tropica*. *L. tropica* infection is not thought to be a widespread cause of chronic symptoms among veterans because there have been no further cases in eight years and because all but one infected veteran clear signs of disease that would be obvious on examination by a doctor mainly a raised temperature and an enlarge liver or spleen.

Prior to the deployment of massive numbers of U.S. troops to this region of the world, viscerotropic leishmaniasis had not been identified in local inhabitants or in the large population of foreign guest workers. However, cutaneous leishmaniasis is a relatively frequent problem in this region. This infection of the skin, which causes a characteristic skin rash, has been diagnosed in 20 U.S. Gulf War veterans.

None of the other endemic infectious diseases that troops encountered during this wartime deployment are likely causes of chronic health problems in U.S. service-members after they returned home. Additionally, in over 100,000 clinical registry health examinations and an epidemiological study conducted by the CDC, no indication was found for any infectious disease as a cause of chronic symptoms. Moreover, a characteristic sign of an infectious process or immune dysfunction has not been identified in registry examinations conducted by VA and DoD.

Mycoplasma Infection

In addition to chronic leishmaniasis, there have been two unconfirmed hypotheses that chronic bacterial infections are the cause of long-term health problems among Gulf War veterans. One hypothesis involves possible infection with the *Mycoplasma* bacterium, either as a natural infection (possibly facilitated by crowding during deployment) or as a genetically engineered biological warfare (BW) agent. A well-know cancer researcher whose stepdaughter developed an unexplained illness after returning from the Gulf War developed this hypothesis. There also have been reports by individual veterans that their chronic symptoms improve with tetracycline and doxycycline

antibiotic therapy. In one published study, however, no association was found between *Mycoplasma fermentans* infection and either deployment to the Gulf region or postwar symptoms.

The other hypothesis involves the possibility of an ongoing (chronic) bacterial infection. This hypothesis originated from pre-Gulf war observations of a doctor who noted that patients with chronic unexplained illnesses, like chronic fatigue syndrome, seemed to respond to antibiotic therapy. Interestingly, this same hypothesis was first proposed in 1915 to explain chronic health problems among military personnel.

These two hypotheses of a chronic bacterial infection are being investigated in separate antibiotic treatment tests. In one study that will cost about twelve million dollars, a double-blind treatment trial has been instituted by the VA as a multi-site study at 30 VA and DoD clinical centers. Either the antibiotic doxycycline or placebo will be given over a 1-year period to approximately 450 veterans who test positive for *Mycoplasma*. Study participants will be followed for changes in their health and symptoms, including fatigue and neurocognitive problems. In the other treatment trial, which received three million dollars in funding from the U.S. Congress, various antibiotics are being administered to Gulf War veterans with unexplained symptoms.

If a favorable response is found in either of these treatment trials, further study will be necessary before antibiotic therapy can be recommended for the treatment of Gulf War veterans. First, the results will have to be independently verified. Secondly, the mechanism of action of antibiotic therapy will have to be determined; that is, whether the response is due to the elimination of a specific infectious agent or whether the effect is due to some other action of drug therapy. Lastly, further research will be necessary to determine the most effective treatment regimen.

A final hypothesis put forward to explain chronic health problems among Gulf War veterans involves possible undetected exposure to biological warfare (BW) agents. However, there was no evidence of biological agents in the Gulf War. A biologic agent was not isolated during the conflict, and most BW agents are designed to be deadly in very small quantities, but there was no cluster of combat casualties consistent with exposure to highly lethal biological weapons like anthrax spores or botulinum toxin.

Conclusion

In conclusion, many health studies consistently show that Gulf War veterans are experiencing a wide range of health problems. Infectious diseases, however, have not been shown to be a major cause of chronic illnesses. After ten years of intense medical observation and study, it is increasingly unlikely that an infectious or immune process could cause serious health problems and yet remain undetected.

Although infectious diseases have not been a major problem, occult (hidden) leishmanial infection could show up over time among a few Gulf War veterans. Leishmaniasis should therefore be considered when suggested by a doctor for clear signs

of infection. Diagnosis may require repeated and painful tissue sampling of bone marrow or lymph nodes to identify the parasite because currently there is no accurate skin or blood test. Treatment for visceral leishmaniasis can be toxic and is not recommended unless the infection is causing chronic health problems.

This article was adapted from a paper prepared by Capt. Kenneth Craig Hyams, M.D., M.P.H., Epidemiology Department, Naval Medical Research Center, for the soon to be published VA Continuing Medical Education program on Gulf War veterans' illnesses.

