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## **AGENT ORANGE AND PERIPHERAL NEUROPATHY**

### **What is peripheral neuropathy?**

Peripheral neuropathy is a nervous system condition that causes numbness, tingling, and muscle weakness by involvement of the peripheral nervous system, that is, nerves outside the brain and spinal cord.

### **Why are Vietnam veterans concerned about peripheral neuropathy? Does Agent Orange/dioxin cause it?**

Some Vietnam veterans have been diagnosed with peripheral neuropathy and others have expressed concern about developing this condition. Some scientific literature has linked peripheral neuropathy to exposure to dioxin, which was contained in Agent Orange.

On May 23, 1991, the Veterans' Advisory Committee on Environmental Hazards considered the relationship between exposure to dioxin and the development of this condition. The Committee concluded that there is a "significant statistical association" between peripheral neuropathy and exposure to dioxin. The Committee qualified this opinion, stating that the association could be said to exist in the absence of exposure to chemical substances known to cause this disorder. Committee members indicated that other risk factors that must be considered are age and whether the individual suffers from other known causes of peripheral neuropathy such as diabetes, alcoholism, or Guillain-Barre syndrome. The Committee also advised that the disorder must become manifest within ten years of the last known dioxin exposure.

### **What did the Department of Veterans Affairs (VA) do in response to the Advisory Committee's finding and the subsequent report released by the National Academy of Sciences in July 1993?**

On July 1, 1991, Secretary of Veterans Affairs Derwinski announced that VA will propose rules granting service-connected disability status to certain veterans with peripheral neuropathy. Proposed rule implementing the Secretary's decision was published for public comment in the Federal Register in January 1992. (See 57 Fed. Reg. 2236, January 21, 1992). It

was anticipated that the final rule would be published in 1993. However, in July 1993, when the National Academy of Sciences (NAS) released its comprehensive report, entitled

**Veterans and Agent Orange -**

**Health Effects of Herbicides Used in Vietnam**, peripheral neuropathy was not included in the category "sufficient evidence of an association" or even "limited/suggestive evidence of an association." Rather, the NAS reviewers concluded that there is "inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides (2,4-D; 2,4,5-T and its contaminant TCDD; cacodylic acid; and picloram) and disorders of the peripheral nervous system." The NAS report added, "Although many case reports suggest that an acute or subacute peripheral neuropathy can develop with exposure to TCDD and related chemicals, reports with comparison groups do not offer clear evidence that TCDD exposure is associated with chronic peripheral neuropathy. The most rigorously conducted studies argue against a relationship between TCDD or herbicides and chronic neuropathy."

Acute is used to mean immediate effect, as opposed to chronic that means an effect not appearing immediately.

VA asked the NAS, in its follow-up report, to consider the relationship between exposure to herbicides and the subsequent development of the acute and subacute effects of peripheral neuropathy (as compared to the chronic effects, which were focused on in the initial report).

In January 1994, VA published a notice in the Federal Register that Secretary Brown has determined that a presumption of service connection based on exposure to herbicides used in Vietnam is not warranted for a long list of conditions identified in the NAS report. Peripheral neuropathy was included in this list. (See 59 Fed. Reg. 341, January 4, 1994).

**What did the NAS 1996 update conclude about peripheral neuropathy?**

When the NAS reviewers separately reviewed **chronic persistent peripheral neuropathy** and **acute and subacute transient peripheral neuropathy**, they found that there was still inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and chronic persistent peripheral neuropathy. On the other hand, they reported that there is some evidence to suggest that "neuropathy of acute or subacute onset may be associated with herbicide exposure." They included acute and subacute transient peripheral neuropathy among those conditions they placed in

their second category "limited/suggestive evidence of an association." (Chronic persistent peripheral neuropathy remained in category three, "inadequate/insufficient evidence to determine whether an association exists.")

**What was VA's response to the NAS 1996 finding about acute and subacute transient peripheral neuropathy?**

After careful review of the report, Secretary Brown decided that VA should add acute and subacute peripheral neuropathy (when manifested within one year of exposure) to the list of conditions recognized for presumption of service connection for Vietnam veterans based on exposure to herbicides. President Clinton announced this, along with other, decisions, at the White House, on May 28, 1996. The proposed rule was published for public comment in the Federal Register in August 1996. (See 61 Fed. Reg. 41368, August 8, 1996). The final rule was published in the Federal Register in November 1996. (See 61 Fed. Reg. 57587, November 7, 1996).

**What did subsequent NAS updates conclude about peripheral neuropathy?**

With regard to chronic persistent peripheral neuropathy, the 1998 report stated, "No new information has appeared in the intervening two years that alters this (the 1996) conclusion."

With regard to acute and subacute transient peripheral neuropathy, the 1998 update reported, "The committee is aware of no new publications that bear on this issue. If TCDD were associated with the development of transient acute and subacute peripheral neuropathy, the disorder would become evident shortly after exposure. The committee knows of no evidence that new cases developing long after service in Vietnam are associated with herbicide exposure."

In update 2000: For chronic persistent peripheral neuropathy, there is only inadequate or insufficient evidence to determine whether an association exists between exposure to dioxin or the herbicides studied in this report. NAS found that there was limited/suggestive evidence of an association between exposure to the herbicides considered in this report and acute or subacute transient peripheral neuropathy. The evidence regarding association was drawn from occupation and other studies in which subjects were exposed to a variety of herbicides and herbicides components. Information available to NAS continued to support this conclusion.

The 2002 update concluded that there is inadequate or insufficient evidence to determine

whether an association exists between the chemicals studied and chronic persistent peripheral neuropathy. In relation to acute and subacute transient peripheral neuropathy, the NAS concluded that there was limited or suggestive evidence of an association between chemical exposure and the disease, as stated in the update 1996 report. Update 2002 also indicated that if TCDD were associated with the development of transient acute and subacute peripheral neuropathy, the disorder would become evident shortly after exposure. The NAS was unaware of any evidence that new cases developing long after service in Vietnam that could be attributed to herbicide exposure in Vietnam.

In Update 2004, the NAS concluded that there is "limited or suggestive" evidence of an association between exposure to the components of interest and early onset transient peripheral neuropathy. However, there is "inadequate or insufficient" evidence to determine an association between exposure to the compound of interest and delayed or persistent peripheral neuropathy.

**Where can a veteran get additional information about peripheral neuropathy?**

Information regarding peripheral neuropathy and related matters can be obtained at VA medical center libraries, from the Environmental Health Clinicians at every VA medical center, or from the Environmental Agents Service (131), Department of Veterans Affairs, 810 Vermont Avenue, N.W., Washington, DC 20420.

**Where can a veteran obtain additional information about Agent Orange-related issues?**

The following Agent Orange Brief fact sheets (including the one you are reading) are available on the World Wide Web at [www.va.gov/AgentOrange](http://www.va.gov/AgentOrange): **A1.**Agent Orange - General Information; **A2.**Agent Orange Class Action Lawsuit; **B1.**Agent Orange Registry Program; **B2.**Agent Orange - Health Care Eligibility; **B3.**Agent Orange and VA Disability Compensation; **B4.**VA Information Resources on Agent Orange and Related Matters; **C1.**Agent Orange - The Problem Encountered in Research; **C2.**Agent Orange and Vietnam Related Research - VA Projects; **C3.**Agent Orange and Vietnam Related Research - Non-VA Projects; **D1.**Agent Orange and Birth Defects; **D2.**Agent Orange and Chloracne; **D3.**Agent Orange and Non-Hodgkin's Lymphoma; **D4.**Agent Orange and Soft Tissue Sarcomas; **D5.**Agent Orange and Peripheral Neuropathy; **D6.**Agent Orange and Hodgkin's Disease; **D7.**Agent Orange and Porphyria Cutanea Tarda; **D8.**Agent Orange and Multiple Myeloma; **D9.**Agent Orange and Respiratory Cancers; **D10.**Agent Orange and Prostate Cancer; **D11.**Agent Orange and Spina Bifida; **D12.**Agent Orange and Diabetes; and **D13.**Agent Orange and Chronic Lymphocytic Leukemia. Hard copies can be obtained from local VA medical centers or from the VA Central Office at the Environmental Agents Service (131) Department of Veterans Affairs, 810 Vermont Avenue, N.W., Washington, DC 20420.

At the same Web site you will find copies of past and current issues of the "Agent Orange Review" newsletter and other items of interest.

**This fact sheet was prepared in August 2005 and does not include any subsequent developments.**