

Final review of health problems that may be linked to Agent Orange exposure during Vietnam War

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The latest and final in a series of congressionally mandated biennial reviews of the evidence of health problems that may be linked to exposure to Agent Orange and other herbicides used during the Vietnam War changed the categorization of health outcomes for bladder cancer, hypothyroidism, and spina bifida and clarified the breadth of the previous finding for Parkinson's disease. The committee that carried out the study and wrote this [report](#), *Veterans and Agent Orange: Update 2014*, reviewed scientific literature published between Oct. 1, 2012, and Sept. 30, 2014.

Bladder cancer and hypothyroidism were moved to the category of "limited or suggestive" evidence of an association from their previous positions in the default "inadequate or insufficient" category. A finding of limited or suggestive evidence of an association means that the epidemiologic evidence indicates there could be a link between exposure to a chemical and increased risk for a particular health effect. A finding of inadequate or insufficient evidence indicates that the available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of such a link. For both [bladder cancer](#) and hypothyroidism, new results from a large study of Korean veterans who served in the Vietnam War were compellingly suggestive of an association. In combination with pre-existing supportive epidemiologic findings and substantial biologic plausibility, the new information provided evidence to merit a change in category of

association for these two outcomes.

The committee for the first Veterans and Agent Orange report in 1994 concluded that there was little and inconsistent evidence concerning an association between any birth defects and parental exposure—either mother or father—to herbicides. The committee for the next report, Update 1996, placed spina bifida in the "limited or suggestive" category of association based on preliminary findings from the then ongoing Air Force Health Study. However, to date, a complete analysis of the data from the Air Force Health Study for neural tube defects has not been published. No subsequent studies have found increases in spina bifida with exposure to components of the herbicides sprayed in Vietnam. Contrary to expectation, intensive investigation of possible heritable effects in animal models still has not demonstrated that herbicide exposure of adult males can produce birth defects in their offspring. Taking these factors into consideration, the committee for this final report concluded that the evidence did not merit retaining [spina bifida](#) in the limited or suggestive category of association and downgraded it to the category of "inadequate or insufficient" evidence. This is only the second time that a Veterans and Agent Orange committee has demoted a health outcome to a weaker category of association. The first instance was the move of porphyria cutanea tarda from the "sufficient" category to the "limited or suggestive" category by the committee for Update 1998.

In addition to reviewing the evidence of health problems that may be linked to exposure to Agent Orange and other herbicides, the committee was asked to address the specific question of whether various conditions with Parkinson's-like symptoms should qualify the assignment of Parkinson's disease to the limited or suggestive category of association with herbicide exposure. The committee noted that Parkinson's disease is a diagnosis of exclusion, and therefore, the diagnostic standards for this condition should not be assumed to have been uniform in the

epidemiologic studies that constitute the basis for this association or in the claims submitted by veterans. Consequently, there is no rational basis for exclusion of individuals with Parkinson's-like symptoms from the service-related category denoted as Parkinson's disease. To exclude a claim for a condition with Parkinson's-like symptoms, the onus should be on the U.S. Department of Veterans Affairs (VA) on a case-by-case basis to definitively establish the role of a recognized factor other than the herbicides sprayed in Vietnam.

Given that this is the final report mandated by the Agent Orange Act, the committee developed recommendations for future actions to advance the well-being of Vietnam veterans, including that the VA should continue epidemiologic studies of the veterans; develop protocols that could investigate paternal transmission of adverse effects to offspring; and design a study to focus on specific manifestations in humans of dioxin exposure and compromised immunity, which have been clearly demonstrated in animal models. The committee also called for a careful review of evidence concerning whether paternal exposure to any toxicant has definitively resulted in abnormalities in the first generation of offspring. In addition, the committee formulated recommendations for improved assembly and evaluation of information necessary for monitoring possible service-related health effects in all military personnel, including creating and maintaining rosters of individuals deployed on every mission and linking U.S. Department of Defense and VA databases to systematically identify, record, and monitor trends in [veterans'](#) diseases.

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