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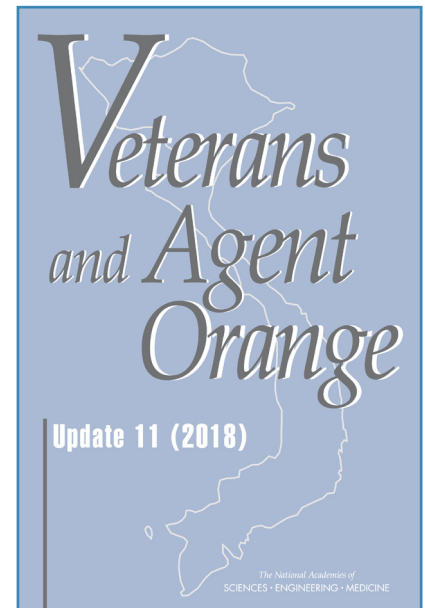
Veterans and Agent Orange

Update 11 (2018)

From 1962 to 1971, the U.S. military sprayed herbicides over Vietnam to strip the thick jungle canopy that could conceal opposition forces, to destroy crops that those forces might depend on, and to clear tall grasses and bushes from the perimeters of U.S. base camps and outlying fire-support bases. The most-used chemical mixture sprayed was Agent Orange, which at the time of use was contaminated with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), the most toxic form of dioxin.

Concerns from Vietnam veterans about their own—and their children’s—health, as well as emerging evidence on ill effects of exposure to Agent Orange, led Congress to enact the Agent Orange Act of 1991. This legislation directed the U.S. Department of Veterans Affairs (VA) to ask the National Academies of Sciences, Engineering, and Medicine to comprehensively evaluate scientific and medical information regarding the health effects of exposure to Agent Orange, other herbicides used in Vietnam, and the various components of those herbicides, including TCDD. The first report, *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam (VAO)*, was published in 1994, and Congressionally mandated updates have been published approximately every 2 years since.

This report, *Veterans and Agent Orange: Update 11 (2018)*, presents the committee’s analysis of peer-reviewed, scientific reports published between September 30, 2014, and December 31, 2017, about associations between various health outcomes and exposure to TCDD and other chemicals in the herbicides used in Vietnam. The report also takes into account information from the existing evidence base.



ABOUT THE STUDY

The committee was asked to determine the following regarding associations between specific health outcomes and exposure to TCDD and other chemicals present in the herbicides used by the military in Vietnam:

- A. whether a statistical association with herbicide exposure exists, taking into account the strength of the scientific evidence and the appropriateness of the statistical and epidemiological methods used to detect the association;
- B. the increased risk of disease among those exposed to herbicides during service in the Republic of Vietnam during the Vietnam era; and
- C. whether there exists a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

The committee was also asked to specifically examine current research available on possible generational health effects, myeloproliferative neoplasms, and glioblastoma multiforme that may be the result of exposures to these chemicals. Importantly, the committee worked independently of the VA and other governmental organizations. It was not asked to, nor did it, make judgments about specific injury cases or provide input on potential compensation policy decisions.

For detailed information about the publications examined by the committee, please visit nationalacademies.org/VeteransAgentOrange2018.

COMMITTEE'S FINDINGS AND RECOMMENDATIONS

VAO committees classify the strength of the evidence regarding the association between exposure to the chemicals of interest and health outcomes into four categories: sufficient, limited or suggestive, inadequate or insufficient, and no association. The classifications are based on the committee's evaluation of the epidemiologic literature and reflect their judgment of the relative certainty of the association between the outcome and exposure to the herbicides used in Vietnam or to any of their components or contaminants.

For a summary of the committee's findings and definitions of the classifications, please see the "Summary Table" document at nationalacademies.org/VeteransAgentOrange2018.

Among the findings, the committee concludes that the information now assembled constitutes sufficient evidence of an association between exposure to at least one of the chemicals of interest and hypertension. This finding is based in part on a recently published study of U.S. Vietnam veterans that found that self-reported hypertension rates were highest among former military personnel who had the greatest opportunity for exposure to these chemicals. The committee also concludes that there is sufficient evidence of an association between exposure and monoclonal gammopathy of undetermined significance, a clinically silent condition that is a precursor to the cancer multiple myeloma.

Relatively few studies have been conducted on the health effects of paternal chemical exposures on their descendants. None to date address Vietnam veterans specifically, and almost all available research was conducted on other populations and has weaknesses that limit its usefulness when assessing risks for veterans. For this reason, the committee strongly believes that more work in this area is warranted, and it recommends further specific study of the health of offspring of male Vietnam veterans.

Myeloproliferative neoplasms and myelodysplastic syndromes are diseases of the blood cells and bone marrow. The committee's search of epidemiologic literature yielded only one relevant paper on these diseases, a study of these cancers in Vietnam veterans that was reviewed in a previous update (*Update 2014*). Because the outcome has not been subject to previous research attention and is of interest to veterans, the committee recommends that investigators examine existing databases on myeloid diseases to determine whether there are data available that would allow for an evaluation of myeloproliferative neoplasms in Vietnam veterans and others who have been exposed to dioxin and the other chemicals of interest.

After conducting a targeted search of the literature related to glioblastoma multiforme and hearing invited presentations from experts in the field, the committee concludes that the evidence of association for exposure to the chemicals of interest and glioblastoma (and other brain cancers) remains inadequate or insufficient. The committee believes it is appropriate for VA be mindful of the concerns raised about the possible association between Vietnam service and glioblastoma. But it observes that the outcome is so rare, and the information concerning herbicide exposures so imprecise, that it is doubtful that any logistically and economically feasible epidemiologic study of veterans would produce meaningful results regarding the association between exposures and the disease. For this reason, the committee recommends that epidemiologic studies of glioblastoma in Vietnam veterans should not be pursued for this purpose and that VA should instead focus on fostering advancements in other areas that may be used to inform improved treatment options.

More generally, the committee notes that although progress has been made in understanding the health effects of military herbicide exposure and the mechanisms underlying these effects, significant gaps in our knowledge remain. Many additional opportunities for progress via continuing and new toxicologic, mechanistic, and epidemiologic research exist. Such work should include efforts to gain new knowledge through the integration of information in existing Department of Defense and VA databases.

CONCLUSION

Despite many criticisms of the conduct of studies of Vietnam veterans' health, including weaknesses and shortcomings in particular papers as well as widespread issues in the literature, the committee wishes to emphasize that the difficulty in conducting research on Vietnam veteran health issues should not act as a barrier to carrying out such work. There are many questions regarding veterans' health that cannot be adequately answered by examining superficially analogous exposures and outcomes in other populations. It is only through research on veterans themselves that the totality of the military service experience can be properly accounted for.

**Committee to Review the Health Effects in Vietnam
Veterans of Exposure to Herbicides (Eleventh Biennial
Update)**

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To read the full report, please visit
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