

AIR FORCE HEALTH STUDY – AN OVERVIEW

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Introduction

In January 1962, the aerial spraying of herbicides in Vietnam, designated Operation Ranch Hand, began. The herbicides sprayed were code-named Herbicide Blue, Green, Pink, Purple, White, and Orange. Although mostly Herbicide Orange was sprayed other dioxin-contaminated herbicides were used, as well as non-dioxin-contaminated herbicides.

In 1970 the aerial spray missions were stopped due to health concerns. In October 1978, the Air Force Deputy Surgeon General made a commitment to Congress and the White House to conduct a health study on the Operation Ranch Hand population. An advisory committee was established to review governmental studies concerned with Vietnam veterans' health.

Materials and Methods

Air Force Health Study Design: The Air Force Health Study protocol was finally approved in 1982 after a rigorous peer review process. The purpose of the Air Force Health Study (AFHS) was to determine whether adverse health outcomes existed among the United States Air Force members (Ranch Hands) assigned to Operation Ranch Hand and could be related to occupational exposure to herbicides, specifically Agent Orange. A prospective cohort study design was used. Three major areas of health outcomes were evaluated – morbidity, mortality, and reproductive health. The morbidity component consisted of six comprehensive physical examinations.

A process was established which identified the 1,245 Ranch Hand personnel who served in Southeast Asia (SEA) between 1962 and 1971. USAF C-130 flight crew and maintenance personnel who were stationed in Southeast Asia at the same time as the Ranch Hands became the Comparison group. Comparison veterans spent on average less than 30 percent of their SEA service in Vietnam and were stationed in Guam, Japan, the Philippines, Taiwan, and/or Thailand.

Because the protocol authors were concerned about differential compliance a strategy was developed to match Comparisons to a Ranch Hand, based on age, race, and military occupation (officer, enlisted flyer and enlisted groundcrew). As many as 10 Comparisons were identified for each Ranch Hand. The purpose of identifying multiple Comparisons was an attempt to maintain the size of the Comparison group when a previously chosen Comparison declined to participate in a subsequent follow-up physical examination.

Mortality Component: The mortality component examined the cause of death of Ranch Hands and the larger Comparison population of slightly more than 20,000, and addressed non-combat mortality from the time of the SEA assignment.

Morbidity Component: The morbidity component analyzed the results of six comprehensive physical examinations conducted in 1982, 1985, 1987, 1992, 1997, and 2002. The medical history of each participant was reconstructed by reviewing and coding past external medical records. Table 1 shows by examination year the attendance for Ranch Hands and Comparisons.¹ Additionally, during the course of the six examinations over 80,000 biological specimens – serum, semen, urine, whole blood, and adipose tissue – were collected.

Table 1. Participation at the AFHS physical examinations.

Group/Examination	1982	1985	1987	1992	1997	2002
Ranch Hands	1,046	1,017	996	953	870	777
Comparisons	1,223	1,292	1,298	1,280	1,251	1,174
Total Participants	2,269	2,309	2,294	2,233	2,121	1,951

For the 1982, 1985, and 1987 physical examinations, the major focus of the analyses was to compare the health status of the Ranch Hands with that of the Comparisons. Methodology to measure dioxin body burden, a surrogate for herbicide exposure, in serum was not available until February 1987. A set of dioxin analyses was performed on the 1987 samples. In 1992, 1997, and 2002 the analyses were focused on group differences between the Ranch Hand and Comparison cohorts and the association of each health endpoint with an extrapolated initial and 1987 serum dioxin level.

Reproductive Component: The possibility of an increased risk in birth defects in children of Vietnam veterans has caused veterans, the general public, and federal and state legislatures concern about possible dioxin exposure received by veterans during the Vietnam War. At the AFHS baseline examination in 1982, reproductive outcome information was collected. A review of birth certificates, newborn clinic records, health records, and death certificates was conducted. The health status of each child was verified through the age of 19. A total of 1,098 Ranch Hands and 1,549 Comparisons fathered 8,263 pregnancies and 6,792 live births. A dioxin level had been determined by August 1991 for 791 Ranch Hands and 942 Comparisons; 5,489 pregnancies and 4,514 live births were fathered by these veterans. A full report was released in August 1992 that described the results of the analysis of reproductive outcomes in conjunction with serum dioxin levels.²

Strengths and Limitations of the Study: AFHS strengths and limitations were codified as follows:

Strengths: 1) High level of Ranch Hand and Comparison participation; 2) existence of a biomarker for exposure to dioxin and herbicides of interest; 3) long follow-up period; 4) six physical examinations over a 20-year period; 5) medical record verification of health conditions; 6) rigorous quality control; 7) independently appointed and administered advisory committee; 8) periodic review by the National Academy of Sciences; 9) two-tiered management structure – parallel program management and technical teams; and 10) adjustment for known confounding factors.

Limitations: 1) Findings cannot be generalized to all Vietnam veterans; 2) sample size not adequate to detect small to moderate increases in rare diseases; 3) serum dioxin measured over 15 years after exposure; and 4) possible incomplete adjustment due to unknown confounding factors.

Results and Discussion

Reproductive Outcomes: There was no meaningful elevation in risk for spontaneous abortion or stillbirth. There were some elevations in risk in some birth defect organ system categories that were not

considered biologically meaningful. There was no indication of increased birth defect severity, delays in development, or hyperkinetic syndrome with paternal dioxin. No associations were seen between paternal dioxin level and intrauterine growth retardation. The risk of infant death was increased among children of Ranch Hands whose fathers had the highest dioxin levels and among children whose fathers had background dioxin levels, but the pattern of results implied that the outcomes might not be related to paternal dioxin levels. No consistent or meaningful associations between serum dioxin levels and testosterone, follicle-stimulating hormone, luteinizing hormone, testicular abnormalities, and testicular volume were observed.

Mortality: An evaluation of post-service mortality through December 31, 2003 found an increased relative risk of all causes and circulatory system mortality in all Ranch Hands and in Ranch Hand enlisted ground crew, the subgroup with highest dioxin levels.³ These results were consistent with the previous AFHS mortality report,⁴ but increases for all Ranch Hands and not only enlisted ground crew were statistically significant. No increase in cancer mortality was observed. These analyses, that included all 20,343 veterans, could only be adjusted for age and military occupation.

Morbidity: No evidence of chloracne was found. The prevalence of cardiovascular disease does not appear to be associated with dioxin exposure. Although there was increased cardiovascular mortality, there was no increase in prevalence of cardiovascular disease. There was some limited support of an association between dioxin levels and neurological disease related to the peripheral nerves. Although differences between groups and associations with dioxin were seen in the psychological tests performed across the six examinations, no clear patterns were discernible. There did not appear to be any clear evidence of psychological disorders or syndromes that could be associated with exposure to herbicides and dioxin. Body mass index was positively associated with 1987 dioxin, possibly reflecting the pharmacokinetics of dioxin elimination.

Results from the 1987, 1992, 1997, and 2002 examinations showed a consistent and potentially meaningful adverse relation between dioxin levels and diabetes. Although the prevalence of diabetes was comparable in Ranch Hands and Comparisons, the assessment of glucose metabolism showed the possibility of adverse effects from dioxin in relation to glucose intolerance and insulin production.⁵

Future of the AFHS Data and Specimens: The U.S. Congress published the Veterans Benefits Act of 2003 in December of that year. In the Act was a section directing the Department of Veterans Affairs to conduct a study to determine 1) if AFHS records, specimens and other data should be retained and maintained; 2) if there were any obstacles to this; 3) if independent oversight of AFHS assets was advisable; 4) the value and relevance of extending the study, potential costs and what entity would be best suited to be the new custodian; and 5) whether or not the specimens should be made available for independent research.

In 2006 the final report was released. This report recommended the retention of the AFHS assets as well as several institutions that would be good custodial candidates. Additionally, it was recommended the implementation of a five-year research plan during which AFHS data/specimens would be made available to the research community.⁶

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