HERBICIDE EXPOSURE AND HEART DISEASE IN VETERANS OF OPERATION RANCH HAND

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Introduction

This report summarizes a study of cardiovascular disease and exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) in veterans of Operation Ranch Hand, the unit responsible for the aerial spraying of herbicides, including Agent Orange, in Vietnam from 1962 to 1971. These results were accumulated during the post-service period from each veteran's departure from Southeast Asia to January 6, 1999 in men participating in the 1997 physical examination in the ongoing Air Force Health Study, a 20-year prospective study of the health, mortality and reproductive outcomes of Ranch Hand veterans. This report is derived from a more extensive summary of the relation between cardiovascular disease and related conditions in men who participated in the latest physical examination of the Air Force Health Study[1].

Methods

The study seeks to determine whether veterans of Operation Ranch Hand (the personnel tasked with spraying operations during the Vietnam conflict) have experienced adverse health and whether those health effects, if they exist, can be attributed to exposure to herbicides or their dioxin contaminant. Ranch Hand veterans were exposed to herbicides during flight operations and maintenance of the aircraft and herbicide spray equipment. The study compares the current health and cumulative mortality experience of Ranch Hand veterans with a comparison group of other Air Force veterans who served in Southeast Asia during the same period (1962 to 1971) that the Ranch Hand unit was active and who were not involved with spraying herbicides. Comparisons were matched to Ranch Hands on age, race and military occupation. The study includes periodic analyses of noncombat mortality, in-person interviews and physical examinations. Physical examinations were conducted in 1982, 1985, 1987, 1992 and 1997; an additional examination is planned for 2002.

In 1987, blood from willing participants was collected and assayed for dioxin. Participation was voluntary and consent forms were signed at the examination site. Veterans with no quantifiable dioxin result in 1987, those who refused in 1987 and subjects new to the study were also asked to give blood for the assay at the 1992 and 1997 examinations. During the baseline, 1985, 1987, and 1992 examinations, each participant was asked whether he had a heart condition. Medical records were sought to verify all reported conditions and to determine the time of occurrence of major cardiac events. Data collected in a similar fashion at the 1997 examination was verified and combined with data from the four previous examinations to create a lifetime history for essential hypertension, heart disease, myocardial infarction, and stroke or transient ischemic attack. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes were used to define these four conditions. Here we report only heart disease (excluding essential hypertension), diagnosed during the post-Vietnam period from the end of the veteran's last tour of duty to January 6, 1999, defined by ICD-9-CM codes 391.0-391.9, 392.0, 393.0-398.99, 402.0-402.91, 404.0-404.9, 410.0-417.9, and 420.0-429.9, which include rheumatic fever with heart involvement, chronic rheumatic heart disease, hypertensive heart disease, ischemic heart disease

and diseases of pulmonary circulation, and other forms of heart disease. This analysis includes all veterans who participated in the most recent physical examination in 1997.

We report two series of analyses. In the first we use exposure group (Ranch Hand, Comparison) as the exposure metric, and in the second we define exposure categories based on exposure group and dioxin levels in serum.

The first series of analyses also includes separate contrasts between exposure groups for each military occupation category (officer, enlisted flyer, and enlisted ground). The separate contrasts are included because enlisted ground personnel have the highest dioxin levels and presumably have experienced the greatest exposure to herbicides. Enlisted flyers have intermediate dioxin levels and officers have the lowest. The total sample sizes for the first series were Comparison: 1,251 and Ranch Hand: 870. After excluding veterans with heart disease before their service in Southeast Asia, the resultant sample sizes for the first series of analyses were Comparison: 1,232 (Officer: 484, Enlisted Flyer: 186, Enlisted Ground: 562) and Ranch Hand: 859 (Officer: 334, Enlisted Flyer: 149, Enlisted Ground: 376).

For the second series of analyses (based on dioxin levels), we excluded veterans with no dioxin measurement, those with a nonquantifiable dioxin result and Comparisons with a dioxin result greater than 10 parts per trillion (ppt), the value we regard as a threshold for background dioxin exposure. Table 1 shows sample size reductions by exposure group (Ranch Hand, Comparison).

Table 1 Sample Size Reduction by Group

	Ranch Hand	Comparison	Total
Fully Compliant in 1997	870	1,251	2,121
Missing or nonquantifiable Dioxin	(7)	(19)	(26)
Comparison Dioxin > 10 ppt	(0)	(19)	(19)
Net	863	1,213	2,076

We defined a categorical index of herbicide and dioxin exposure based on dioxin measurements in serum. We estimated the initial dioxin dose at the end of the tour of duty in Vietnam in Ranch Hands having measured dioxin levels above background using a constant half-life of 8.7 years and assigned each veteran to one of four exposure categories, named "Comparison", "Background", "Low" and "High", according to his group, measured dioxin level and initial dioxin level. The Comparison category was comprised of Comparisons with dioxin levels less than or equal to 10 ppt. The Background category was comprised of Ranch Hands with dioxin levels less than or equal to 10 ppt. Ranch Hands with dioxin levels greater than 10 ppt were assigned to the Low or High categories depending on their estimated initial dioxin level. The cut point separating the Low and High categories (94 ppt) is the median initial dioxin level among all Ranch Hands having measured dioxin levels greater than 10 ppt. The resultant sample sizes were Comparison: 1,213, Background: 381, Low: 239, High: 243. After excluding veterans with heart disease before their service in Southeast Asia, the resultant sample sizes for the second series of analyses were Comparison: 1,195, Background: 376, Low: 233, High: 243.

In both the occupation-based analysis and the dioxin category analysis, we excluded veterans with heart disease before their service in Southeast Asia. The resultant sample sizes were Comparison: 1,232 (Officer: 484, Enlisted Flyer: 186, Enlisted Ground: 562), Ranch Hand: 859 (Officer: 334, Enlisted Flyer: 149, Enlisted Ground: 376). The dioxin category final sample sizes were Comparison: N=1,195, Background: N=376, Low: N=233, High: N=243.

We defined percent body fat (PBF) as PBF=1.26×BMI-13.305, where BMI is the body mass index [weight (kg) divided by the square of height (m)] and adjusted all analyses for age, military occupation (officer, enlisted flyer, enlisted ground), lifetime cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, diabetic class, body fat, personality type, family history of heart disease before the age of 45, and taking blood pressure medication. We report cumulative incidence, or prevalence, of heart disease by group and occupational stratum, and dioxin category. We measured the association between heart disease prevalence and exposure category with the adjusted odds ratio (aOR) and assessed the precision of the estimate with a 95% confidence interval (95% CI) for the aOR. We derived the aOR and its confidence interval from a main effects logistic regression model containing dioxin category and all covariates. In the analysis based on dioxin exposure category, we compared the heart disease prevalence among Ranch Hand veterans in the Background, Low and High categories with Comparison veterans. We used no stepwise reduction in either analysis.

Results and Discussion

Demographic characteristics of all veterans in 1997 are presented in Table 2 by dioxin exposure category. Ranch Hands in the High dioxin category are younger than Ranch Hands in the Low and Background categories.

Table 2. Distribution of dioxin and demographic characteristics in 1997

Characteristic	Comparison (N=1,213)	Background (N=381)	Ranch Hand Low (N=239)	High (N=243)
Dioxin*	3.8 (0-9.97)	5.8 (0-10)	15 (10.0-25.6)	45.7 (18.0-617.8)
Initial dioxin*			51.8 (27.7-93.8)	194.7 (94.0-3290)
Age in 1997*	57.6 (46.7-82.5)	59.6 (46.9-77.5)	60.7 (47.0-79.3)	52.4 (47.2-76.6)
PBF in 1997*	22.6 (7.1-52.6)	20.7 (9.4-44.6)	22.9 (7.1-47.8)	23.3 (12.9-45.9)
Race (Black)†	5.8	5.0	9.6	5.3
Officer†	39.4	61.4	40.2	2.9
Enlisted flyer†	15.3	12.6	21.3	21.4
Enlisted Ground†	45.3	26.0	38.5	75.7

*Median (Range) † Percent.

The percentage of Ranch Hand veterans with heart disease (66.1%) is increased relative to Comparisons (60.8%); aOR=1.3, 95% CI 1.0, 1.5 (Table 3). The risk of heart disease is increased in all three occupational categories, with the greatest increase occurring among enlisted flyers..

Table 3. Heart Disease by Occupational Category

Occupational Category	Group	N	Number (%)	aOR (95% CI)
All	Ranch Hand	859	568 (66.1)	1.3 (1.0, 1.5)
	Comparison	1,232	749 (60.8)	
Officer	Ranch Hand	334	238 (71.3)	1.2 (0.9, 1.7)
	Comparison	484	324 (66.9)	
Enlisted Flyer	Ranch Hand	149	112 (75.2)	2.1 (1.3, 3.5)
	Comparison	186	111 (59.7)	
Enlisted Ground	Ranch Hand	376	218 (58.0)	1.1 (0.8, 1.5)
	Comparison	562	314 (55.9)	

The percentages of Ranch Hands in the Background (aOR=1.3) and Low (aOR=1.3) dioxin categories having heart disease are increased relative to the Comparisons (Table 4).

Table 4. Heart Disease by Dioxin Exposure Category

		Ranch Hand		
	Comparison	Background	Low	High
Number (%)	730 (61.1)	259 (68.9)	163 (70.0)	139 (57.2)
aOR	1.0	1.3	1.3	1.0
95% CI		(1.0, 1.8)	(1.0, 1.8)	(0.8, 1.4)

The study is limited by incomplete knowledge of dioxin exposure. We are uncertain about the exposure status of Ranch Hands in the Background category; some of these veterans could have received elevated dioxin levels in Vietnam but their body burden decreased to background levels in the intervening time period, and some may not have received an elevated level during their service in the Ranch Hand unit, causing us to misclassify some of them. However, a recent study of skin exposure to herbicides in Ranch Hand enlisted veterans showed that veterans assigned to administrative duties and those reporting no skin exposure had the lowest measured dioxin levels (approximately 60% had background levels) and more than 75% of those reporting high skin exposure had measured dioxin levels above background. Thus, it appears that most Ranch Hand veterans with background levels were probably unexposed or received minimal exposure to herbicides in Vietnam. More specific statements about Ranch Hand veterans having background dioxin levels are not possible based on available data.

Reference

1. Michalek, J.E., Burnham, B.R., Marden, H.E., et al. (2000). The Air Force Health Study. 1997 Follow-up Examination Results. National Technical Information Service: Springfield.