

**SERUM DIOXIN AND CANCER
IN VETERANS OF OPERATION RANCH HAND**

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Introduction

This report summarizes a study of cancer 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 1971¹. These results were accumulated during the post-service period from each veteran's departure from Southeast Asia to June 15, 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.

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 could have been 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, the index group, 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. The study includes in-person interviews and physical examinations and serum dioxin measurements. Physical examinations were conducted in 1982, 1985, 1987, 1992 and 1997.

We defined cancer as a malignant neoplasm and considered all occurrences of cancer during the entire post-service period from the end of each veteran's service in Southeast Asia to June 15, 1999 in all veterans who participated in the 1997 physical examination. Information on the occurrence of cancer was collected in questionnaires and physical examinations. All reported conditions were verified by medical record review and double blind medical coding by certified medical record specialists with independent adjudication of discordances. Conditions verified from medical records were coded according to the conventions of the International Classification of Diseases, 9th Revision, Clinical Modification manual.

We excluded veterans with cancer prior to service in Vietnam, those with a missing dioxin measurement, or a dioxin measurement we could not quantify. We also excluded Comparison veterans having a dioxin result greater than 10 parts per trillion (ppt), the value we regard as a threshold for background dioxin exposure. The sample size reduction is summarized in Table 1.

Table 1 Study Size Reduction

	Ranch Hand	Comparison	Total
Attended 1997 physical exam	870	1251	2121
Missing or nonquantifiable dioxin	(7)	(19)	(26)
Comparison dioxin>10 ppt		(19)	(19)
Net	863	1213	2076

Because exposure to ultraviolet light is a primary cause of basal cell carcinoma, we computed a cumulative sun-exposure index based on lifetime residential history. We estimated an average residential latitude by dividing the total degree-years (the sum of the product of the latitude and the number of years lived at each residence) from all of the residences by the total number of reported residential years spanning the entire life time of each veteran. We defined percent body fat (PBF) as $PBF=1.264 \times BMI - 13.305$, where BMI is the body mass index [weight (kg) divided by the square of height (m)]. We computed PBF using the weight and height measured at the physical examination during which the veteran gave blood for the dioxin measurement. We defined a pack-year as smoking one pack of cigarettes per day for one year and a drink-year as drinking one shot of 80 proof whiskey per day for one year.

We restricted analyses of skin cancer to nonblack veterans and adjusted for age, military occupation (officer, enlisted flyer, enlisted ground personnel), skin color (dark, medium, pale, dark peach, pale peach), hair color (black, dark brown, light brown, blonde, red, bald), eye color (brown, hazel, green, gray, blue), reaction of skin to sun exposure after first exposure (no reaction, becomes red, burns, painfully burns), reaction of skin after repeated exposures (deeply tanned, moderately tanned, mildly tanned, no tan), average lifetime residential latitude, percent body fat at the time of the dioxin blood draw, and exposure to ionizing radiation (yes, no), industrial chemicals (yes, no), herbicides (yes, no), insecticides (yes, no), and degreasing chemicals (yes, no). We included all veterans in analyses of cancer at sites other than the skin and adjusted for birth year, military occupation, race, percent body fat at the time of the dioxin blood draw, lifetime cigarette smoking (pack-years), lifetime alcohol consumption (drink-years), and exposure to asbestos (yes, no), ionizing radiation (yes, no), industrial chemicals (yes, no), herbicides (yes, no), insecticides (yes, no), and degreasing chemicals (yes, no). The units of smoking and drinking are packyears and drinkyears. Age was determined at the 1997 physical examination.

Using a first order model for dioxin elimination and a constant half life of 8.7 years, we extrapolated the measured dioxin to the initial dioxin level at the end of service in Southeast Asia among Ranch Hand veterans having measured dioxin levels greater than 10 ppt. To assess the association between dioxin and cancer, we stratified the data according to group, measured dioxin level and initial dioxin level to four exposure categories named Comparison, Background, Low and High. The Comparison category was comprised of Comparison veterans with measured dioxin less than or equal to 10 ppt. The Background category was comprised of Ranch Hand veterans with measured dioxin less than or equal to 10 ppt. The Low and High categories are comprised of Ranch Hand veterans having measured dioxin greater than 10 ppt, with veterans assigned to the Low category if their initial dioxin was less than or equal to 94 ppt and to the High category if their initial dioxin was greater than 94 ppt, where 94 ppt was the median initial dioxin among those with measured dioxin levels greater than 10 ppt. The resultant sample sizes were Comparison: N=1,213, Background: N=381, Low: N=239, High: N=243. In the analysis of skin cancer, we excluded black veterans and those with skin neoplasms (malignant or otherwise) before their service in Southeast Asia. The resultant sample sizes by dioxin category were

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Comparison: N=1,133, Background: N=359, Low: N=210, High: N=229. In the analysis of cancers at sites other than the skin, we excluded veterans with malignant neoplasms or neoplasms of uncertain nature at sites other than the skin before their service in Southeast Asia (Ranch Hand: N=9, Comparison: N=2). The resultant sample sizes were Comparison: N=1,211, Background: N=378, Low: N=234, High: N=242.

We report cumulative incidence, or prevalence, of cancer by dioxin category. We measured the association between cancer prevalence and dioxin 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. We compared the cancer prevalence among Ranch Hand veterans in the Background, Low and High categories with Comparison veterans. We used no stepwise reduction.

Results and Discussion

Demographic characteristics are summarized in Table 2. Veterans in the High dioxin category were younger on the average and tended to drink less than those in the Comparison category.

Table 2. Distribution of dioxin and demographic characteristics

Characteristic	Comparison (N=1,213)	Ranch Hand		
		Background (N=381)	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)
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)
Lifetime drinking*	20.7 (0-627)	19.8 (0-518)	23.9 (0-412.7)	17.6 (0-507.3)
Lifetime smoking*	8 (0-129)	7 (0-114)	9.8 (0-172)	7 (0-129)
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

Skin cancer and dioxin category are summarized in Table 3. No Black Ranch Hand veterans had skin cancer.

Table 3. Skin cancer in nonblack veterans

	Comparison	Ranch Hand		
		Background	Low	High
Number (%)	179 (15.8)	65 (18.1)	47 (22.4)	32 (14.0)
aOR	1.0	1.1	1.5	1.2
95% CI		0.8, 1.6	1.0, 2.1	0.8, 1.9

Cancer at sites other than the skin and dioxin category are summarized in Table 4.

Table 4. Cancer at sites other than the skin

	Comparison	Ranch Hand		
		Background	Low	High
Number (%)	73 (6.0)	21 (5.6)	34 (14.5)	11 (4.6)
aOR	1.0	0.7	1.9	0.9
95% CI		0.4, 1.3	1.2, 3.2	0.4, 1.8

We found no evidence of a dose-response gradient and no significant increased risk of cancer in the High dioxin category, the subgroup of greatest a priori interest. The prevalence of skin cancer appeared unrelated to dioxin exposure category. For both skin cancer and cancer at sites other than the skin, risk was increased in the Low category. The risk of cancer at sites other than the skin was not increased in the High category. These patterns were not suggestive of an adverse association between dioxin and cancer. Our ability to detect associations was limited by the size of the Ranch Hand group.

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.

