

## SERUM TCDD AND HEMATOLOGICAL EXAMINATION RESULTS IN VETERANS OF OPERATION RANCH HAND

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### Introduction

We studied indices of hematologic function and exposure to 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD) in Vietnam War veterans of Operation Ranch Hand, the Air Force unit responsible for the aerial spraying of Agent Orange and other herbicides in Vietnam<sup>1</sup>. The herbicides were contaminated with TCDD. We measured TCDD serum level in 1987 or later and extrapolated the result to the time of service in Vietnam. We studied serum TCDD level in relation to red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, white blood cell count, platelet count, and erythrocyte sedimentation rate at each of four physical examinations in 1982, 1985, 1987 and 1992. Compared with veterans not involved in Operation Ranch Hand, those with the highest TCDD levels in Operation Ranch Hand had mean corpuscular volumes that were about 1% higher and platelet counts that were about 4% higher. These small increases were unlikely to be of clinical significance and may not have been caused by TCDD.

### Materials and 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 TCDD 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 TCDD measurements.

We report analyses of hematological function and TCDD body burden among veterans who participated in the 1982, 1985, 1987 and 1992 studies. Beginning in 1987, blood from willing veterans was collected and TCDD was measured in serum and expressed as parts per trillion (ppt) serum lipid. TCDD levels less than the limit of detection were assigned the value 0 ppt. Veterans with TCDD levels greater than or equal to the limit of detection but less than the limit of quantitation were excluded from this study; we refer to such values as nonquantifiable. TCDD levels greater than or equal to the limit of quantitation were called quantifiable. Veterans with no quantifiable TCDD result in 1987, those who refused in 1987 and veterans new to the study in

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1992 were invited to give blood for the assay at the 1992 examination. Of the 2,233 veterans who attended the 1992 physical examination, TCDD assays were done for 2,198 (98.4%)<sup>1</sup>.

We excluded veterans with a missing or nonquantifiable TCDD measurement and comparisons with a TCDD result greater than 10 ppt serum lipid, the value we regard as a threshold for background TCDD exposure. Missing TCDD levels were caused by refusal, noncompliance to the physical examination, or a failure of one or more quality control checks and insufficient sample to repeat the analysis. We also excluded veterans who had a fever (body temperature greater than or equal to 100° Fahrenheit) at the time of the examination or tested positive for human immunodeficiency virus (HIV).

We estimated the initial TCDD dose at the end of the tour of duty in Vietnam in Ranch Hands having TCDD levels above background using a constant half-life of 8.7 years. We assigned each veteran to one of four exposure categories, named "Comparison [0, 10]," "Ranch Hand [0, 10]," "Ranch Hand [10, 94]," and "Ranch Hand [94, 3290]." The Comparison [0, 10] category was comprised of Comparison veterans with TCDD less than or equal to 10 ppt. The Ranch Hand [0, 10] category was comprised of Ranch Hand veterans with TCDD level less than or equal to 10 ppt. Ranch Hands with TCDD>10 ppt were assigned to the Ranch Hand [10, 94] and [94, 3290] categories, where the cut point was the median estimated initial TCDD level at their departure from Southeast Asia (94.0 ppt). Table 1 shows study size reductions by group (Ranch Hand, Comparison) and examination year.

Table 1. Sample Sizes by Group and Examination Year

Group	Stratum	Examination Year			
		1982	1985	1987	1992
Ranch Hand	Compliant	1,046	1,017	996	953
	Fever	(9)	(2)	(1)	(3)
	HIV positive	(5)	(5)	(4)	(3)
	Missing TCDD	(100)	(61)	(33)	(19)
	Nonquantifiable TCDD	(3)	(5)	(5)	(3)
	Net	929	944	953	925
	Ranch Hand [0,10]	384	400	404	398
	Ranch Hand [10, 94]	271	269	276	262
Ranch Hand [94, 3290]	274	275	273	265	
Comparison	Compliant	1,223	1,292	1,298	1,280
	Fever	(2)	(1)	(3)	(1)
	HIV positive	(1)	(1)	(1)	(1)
	Missing TCDD	(123)	(84)	(40)	(33)
	Nonquantifiable TCDD	(24)	(27)	(29)	(24)
	TCDD>10 ppt	(24)	(25)	(25)	(24)
	Comparison [0,10]	1,049	1,154	1,200	1,197

At each examination, we measured red blood cell count ( $10^6/\text{mm}^3$ ), hemoglobin (g/dl), hematocrit (%), mean corpuscular volume ( $\mu\text{m}^3$ ), white blood cell count ( $10^3/\text{mm}^3$ ), platelet count ( $10^3/\text{mm}^3$ ), and the erythrocyte sedimentation rate (mm/hr). All measurements were determined by a Coulter

STKS Analyzer. The 1982 examination was conducted in Houston, Texas and the 1985, 1987 and 1992 examinations were conducted in San Diego, California. Platelet count means are tabulated by examination year and exposure category.

We estimated percent body fat (PBF) as  $PBF = 1.26 \times BMI - 13.305$ , where BMI is the body mass index [weight (kg) divided by the square of height (m)]. We defined a pack-year as smoking one pack of cigarettes per day for one year. We adjusted all analyses for PBF, age, race (Black, nonblack), military occupation (officer, enlisted flyer, enlisted ground crew) and lifetime cigarette smoking (pack-years).

We used a linear model to estimate adjusted mean differences between the Comparison [0, 10] and each of the three Ranch Hand TCDD categories ([0, 10], [10, 94], [94, 3290]) for each laboratory measurement. We report adjusted least square means, differences of least square means, and the 95% confidence interval (95% CI) for the difference of least square means.

## Results and Discussion

Demographic characteristics of these veterans at the 1987 physical examination are presented in Table 2. Most Ranch Hands in the [94, 3290] TCDD category were enlisted ground personnel while most in the [0, 10] category were officers. Ranch Hands in the [94, 3290] TCDD category were younger and smoked more on the average than Ranch Hands in both the [0, 10] and [10, 94] categories.

**Table 2.** Distribution of TCDD and demographic characteristics

Characteristic	Comparison	Ranch Hand		
		[0, 10]	[10, 94]	[94, 3290]
TCDD Median (range)	4.0 (0, 10)	5.7 (0, 10)	51.7 (27, 94)	194.7 (94, 3,290)
Age (years) Mean (sd)	48.8 (7.6)	50.0 (7.3)	50.3 (7.7)	46.4 (7.3)
Race (% Black)	5.7	5.0	8.7	4.8
PBF Mean (sd)	21.8 (5.1)	20.1 (4.4)	22.2 (5.3)	23.3 (5.6)
Current Smoker (%)	30.8	33.7	33.7	38.5
Military Occupation:				
Officer (%)	38.0	62.1	38.8	2.9
Enlisted Flyer (%)	16.3	11.9	20.7	22.0
Enlisted Grd Crew (%)	45.7	26.0	40.6	75.1

The mean platelet count (Table 2) was significantly increased in the Ranch Hand [94,3290] category in 1982 (Ranch Hand mean=278.66  $10^3/\text{mm}^3$ , Comparison mean=262.23  $10^3/\text{mm}^3$ , mean difference=16.43  $10^3/\text{mm}^3$ , 95% CI 8.44 to 24.41), 1987 (Ranch Hand mean=263.09  $10^3/\text{mm}^3$ , Comparison mean=254.52  $10^3/\text{mm}^3$ , mean difference=8.57  $10^3/\text{mm}^3$ , 95% CI 0.92 to 16.22), and 1992 (Ranch Hand mean=255.14  $10^3/\text{mm}^3$ , Comparison mean=244.46  $10^3/\text{mm}^3$ , mean difference=10.68  $10^3/\text{mm}^3$ , 95% CI 3.19 to 18.16).

**Table 3.** Platelet count means by TCDD category and examination year.

		Comparison	Ranch Hand		
			[0, 10]	[10, 94]	[94, 3290]
1982	Mean	262.23	271.42	269.11	278.66
	Difference		9.19	6.88	16.43
	95% CI		2.27, 16.12	-0.85, 14.61	8.44, 24.41
1985	Mean	261.99	265.25	262.67	267.77
	Difference		3.27	0.68	5.78
	95% CI		-3.31, 9.84	-6.81, 8.18	-1.92, 13.49
1987	Mean	254.52	258.16	258.21	263.09
	Difference		3.63	3.68	8.57
	95% CI		-2.87, 10.14	-3.69, 11.06	0.92, 16.22
1992	Mean	244.46	246.83	246.84	255.14
	Difference		2.36	2.37	10.68
	95% CI		-3.92, 8.65	-4.89, 9.63	3.19, 18.16

We found consistent associations between TCDD exposure and increased mean corpuscular volume and increased platelet count. The erythrocyte sedimentation rate was intermittently higher among those with elevated TCDD levels. The average increases in mean corpuscular volume and platelet count associated with TCDD exposure, however, were slight and the clinical significance is unclear. A slight increase in the mean hemoglobin in the Ranch Hand [94, 3290] TCDD exposure category was seen in 1982 only. Results for mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration closely paralleled those of mean corpuscular volume.

Increased platelet count, called thrombocytosis when greater or equal to 500,000/ $\mu$ L, is also associated with a diverse group of conditions including malignancy, tissue damage, acute or chronic inflammation, certain drugs, and renal disease. The intermittently increased erythrocyte sedimentation rate among those with elevated TCDD levels was suggestive of an inflammatory process, and such a process might also account for the increased platelet count. Among normal men correlates of platelet count include serum cholesterol and hematocrit, but we saw no relation of TCDD with either of these.

In conclusion, we found no consistent relation between TCDD body burden and red blood cell count, hemoglobin, hematocrit, white blood cell count, and erythrocyte sedimentation rate. Mean corpuscular volume and platelet count, however, generally increased with increasing TCDD level at each of four examinations between 1982 and 1992. Whether these associations are due to TCDD exposure cannot be determined with these data.

**Reference**

I. Michalek, J., Akhtar F., Longnecker M., and Burton J. (2001) Arch Environ Health (In press).