

SERUM TCDD LEVELS AND THYROID SYSTEM EFFECTS AMONG US AIR FORCE VETERANS

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Introduction

The Air Force Health Study (AFHS) is a 20-year prospective study of health, mortality and reproductive outcome of Ranch Hand veterans who participated in the aerial spraying of herbicides, including Agent Orange contaminated with TCDD, in Vietnam from 1962 to 1971. The present study examines potential physiological changes and health effects related to thyroid function and whether they could be attributed to TCDD exposure.

Results of animal studies¹⁻⁴, studies in infants⁵⁻⁶ and some occupational studies in chemical workers⁷⁻⁸ suggest that TCDD may be involved in alterations of thyroid function manifested primarily as decrease in thyroxine (T4) and increase in thyroid stimulating hormone (TSH) levels.

In previous reports from the Ranch Hand study, a slight and statistically non-significant increase in the mean TSH level with increasing TCDD level was observed in 1987 and 1992. Here we report blood TSH levels as well as odds ratios for hypothyroidism and all thyroid disease combined in association to serum TCDD levels in these US Air Force veterans.

Methods

The Air Force Health Study (AFHS) compares health status and cumulative morbidity and mortality experience of Ranch Hand Vietnam veterans with a comparison group of other Air -Force veterans who served in Southeast Asia during the same time period but were not involved in spraying herbicides. Details of study design and methods were published elsewhere⁹.

Periodic medical examinations of veterans were conducted in 1982, 1985, 1987, 1992, and 1997. Blood for TCDD measurement for most of the veterans was collected in 1987. Codes 240 to 246 excluding congenital hypothyroidism (243) of the International Classification of Diseases (ICD-9) were used to identify thyroid diseases (240 simple and unspecified goiter, 241 nontoxic nodular goiter, 242 thyrotoxicosis, 244 acquired hypothyroidism, 245 thyroiditis, 246 other disorders of thyroid). In this study, data was available for 2438 veterans (1009 Ranch Hand and 1429 comparison) who participated in at least one physical examination and had a measurement of serum TCDD.

Least square means and test for trends were calculated in linear regression modeling to compare mean thyroid hormone levels at each examination for both groups of veterans. Exposure to TCDD was categorized to quartiles of log-transformed TCDD levels based on distribution in combined veterans' cohort. Unconditional logistic regression was used to report odds ratios and 95% confidence intervals between thyroid disease in Ranch Hand and comparison veterans. Ranch Hand veterans exposure to TCDD was categorized to tertiles of their log-transformed TCDD distribution, comparison group of veterans served as a reference. Linear and logistic models were adjusted for year of birth, body mass index, primary military occupation, and triglycerides level at blood draw.

Results

Personal and demographic characteristics on participants of the study are presented in Table 1. TCDD levels in Ranch Hand veterans were comparable to the comparison veterans in the first tertile [4.8 vs. 3.9 parts per trillion (ppt)], but the median values were three [11.9 vs. 3.9 (ppt)] and ten times [43.4 vs. 3.9 (ppt)] higher in the second and third tertiles.

Table 1. Median TCDD levels and demographic characteristics of veterans at blood draw

Characteristic	Comparison	Ranch Hand		
		1st Tertile	2nd Tertile	3rd Tertile
TCDD [Median (0-100%)]	3.9 (0.3-54.8)	4.8 (0.4-7.8)	11.9 (7.9-20.2)	43.4 (20.3-617.8)
Age (years) [Mean (SD)]	43.9 (7.7)	44.7 (7.3)	45.4 (7.4)	41.1 (7.3)
BMI (kg/m ²) [Mean (SD)]	27.9 (4.1)	26.4 (3.5)	27.8 (3.9)	28.8 (4.4)
Occupation:				
Officer (%)	37.9	61.5	46.5	4.5
Enlisted Flyer (%)	15.8	12.1	18.6	21.2
Enlisted Ground (%)	46.3	26.4	34.9	74.3

We did not observe increased TSH levels in Ranch Hand veterans in association with the increasing serum TCDD levels across five physical examinations for which TSH levels were measured (Table 2). The drop in TSH levels from 1982 to 1985 was caused by a change in laboratory methodology. None of the tests for linear trend reached statistical significance. We also did not find substantial differences between TSH levels of Ranch Hand and comparison veterans. No substantial decrease in levels of T4 was noted in association with TCDD levels in either group of veterans for any examination (data not shown).

Adjusted odds ratios for all thyroid disease combined, ICD-9 codes 240-246, and for acquired hypothyroidism (244) are presented in Table 3. Veterans of operation Ranch Hand did not have higher odds of developing hypothyroidism than comparison veterans. We also did not find elevated odds ratios for hypothyroidism with increasing level of TCDD exposure as measured in 1987. When we combined all ICD-9 codes for thyroid diseases into one category, we did not observe a higher odds among Ranch Hand veterans (Table 3).

Discussion

We do not report any significant associations between thyroid hormone levels (T4 and TSH) or increased odds of hypothyroidism or any thyroid disease developed after return from Southeast Asia. These preliminary results do not include data on repeated TCDD measurements in a subgroup of veterans with higher TCDD levels (n=343) that will be used in our further analyses¹⁰.

The strengths of this study include a very detailed 15-years of follow-up of subjects who participated in study and repeated verifications of their health status and medical records. Inferences that could be made from these data are limited by relatively low levels of serum TCDD in the majority of Ranch Hand veterans and measurement of only one of the dioxin congeners (TCDD). Elevated

TCDD levels were previously reported in Vietnamese and U.S. Vietnam veterans¹¹. TCDD levels in Ranch Hand veterans were lower than in some occupationally exposed workers. Dibenzofurans or polychlorinated biphenyls were not analyzed in this cohort and limit the estimates of total dioxin body burden. Alterations in thyroid function that may have occurred close to time of exposure in Vietnam were probably not documented, and the cohort may not yet be old enough to determine whether TCDD has any effect on prevalence of thyroid disease in older age. Further follow-up of this group of veterans may be required to observe any alteration of thyroid function.

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Table 2. Mean thyroid stimulating hormone (TSH) levels in Air Force veterans by TCDD category and physical examination*

	1982		1985		1987		1992		1997	
	Comp. n=1098	RH n=946	Comp. n=1205	RH n=956	Comp. n=1249	RH n=962	Comp. n=1249	RH n=937	Comp. n=1225	RH n=854
Mean TSH	4.14	4.01	1.49	1.42	1.18	1.11	2.17	2.11	2.29	2.33
TCDD (ppt)										
< 3.27	4.15	3.38	1.56	1.16	1.04	0.84	1.91	1.56	2.18	1.90
3.28-5.07	3.93	4.05	1.39	1.46	1.13	1.19	2.50	2.27	2.22	2.41
5.08-9.87	4.24	4.09	1.53	1.37	1.41	1.10	2.10	2.07	2.54	2.48
> 9.87	3.67	4.06	1.31	1.46	1.10	1.15	1.85	2.18	2.02	2.30
P for trend	0.26	0.13	0.48	0.11	0.69	0.08	0.76	0.24	0.30	0.40

*Comp. - comparison group of Air Force veterans, RH - Ranch Hand veterans; Quartiles based on a TCDD distribution in a combined cohort

Table 3. Adjusted odds ratios for hypothyroidism and all thyroid disease combined in Air Force veterans*

Veterans Group	Hypothyroidism				All thyroid disease			
	Disease (%)	No disease	OR	95% CI	Disease (%)	No disease	OR	95% CI
Comparison	47 (3.4)	1318	1.00	Ref.	111 (7.8)	1318	1.00	Ref.
Ranch Hand	31 (3.2)	932	0.92	0.58-1.46	77 (7.6)	932	0.95	0.58-1.46
Comparison	47 (3.4)	1318	1.00	Ref.	111 (7.8)	1318	1.00	Ref.
Ranch Hand								
1. Tertile (< 7.9 ppt)	10 (3.1)	311	0.89	0.44-1.81	29 (8.5)	311	1.13	0.44-1.81
2. Tertile (7.9 - 20.3 ppt)	11 (3.4)	310	0.95	0.49-1.86	28 (8.3)	310	1.03	0.49-1.86
3. Tertile (>20.3 ppt)	10 (3.1)	311	0.96	0.47-1.96	20 (6.0)	311	0.80	0.47-1.96

*All analyses adjusted for BMI, year of birth, military occupation, and triglyceride levels at the blood draw;
OR – odds ratios