

EXPOSURE PREDICTORS OF 2,3,7,8-TCDD SERUM CONCENTRATION ON VIETNAM-ERA CHEMICAL CORPS VETERANS

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Introduction

Members of the U.S. Army Chemical Corps were responsible for the storage, preparation and spraying of herbicides around the perimeters of base camps and aerial spraying from helicopters during the Vietnam conflict.¹ Although they used a smaller volume of herbicides than the much-studied Ranch Hand cohort, it is hypothesized that substantial exposures may have resulted from more intimate contact with these agents. This study was undertaken as part of a larger health study of the U.S. Army Chemical Corps cohort to determine if current serum concentrations of 2,3,7,8-TCDD were (still) elevated and to determine what activities, if any, relating to service in Vietnam or proximity to herbicide contaminated with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) were predictive of exposure as measured by current serum concentrations.

Methods and Materials

This study was conducted utilizing questionnaire responses and measured serum dioxin congener concentrations in a subset of persons who had served in the U.S. Army Chemical Corps between 1965 and 1973 as identified from a variety of sources.¹ The population for the current study was randomly selected from a larger cohort of living Vietnam-era U.S. Army Chemical Corps veterans (*n* = 5609) assembled for a different study.² Based on analyses of data collected during a pilot study, the study population selection was weighted to over sample persons reporting Vietnam service (*n* = 342 persons reporting Vietnam service; *n* = 54 persons not reporting Vietnam service). From the initial total study population (*n* = 396), 11 subjects were excluded because of missing serum dioxin data and 5 persons were excluded because of uncertain spraying status from the questionnaire, giving a final study population of 380.

Information on service in Vietnam was gathered both by self-report and by Army records. A detailed questionnaire was administered to all study participants to elicit information on historic use of herbicides both in the military and in current or past civilian employment. Questions concerning possible military exposure were devised to determine use of particular herbicides (*e.g.*, Agent Orange, Agent White) by year and country. For each herbicide, the respondent was asked to estimate the frequency and duration of use.

Blood samples were collected at the subjects' homes and were shipped to laboratories at the U.S. Centers for Disease Control and Prevention for dioxin congener analysis using a standardized protocol.³ For the purposes of this study, all exposure analyses were limited to the use of the lipid-corrected 2,3,7,8-TCDD concentration in serum as the outcome measure. Of the 380 members of the study cohort, 66% (n = 252) had serum dioxin concentrations below the analytical limit of detection (LOD). For those persons, the lipid and sample volume corrected 2,3,7,8-TCDD limit of detection concentration divided by two was substituted for subsequent statistical analyses and modeling. All statistical analyses and models used the logarithmic (log) values of the lipid-corrected 2,3,7,8-TCDD concentration or the log values of the LOD divided by two for those concentrations below the LOD.

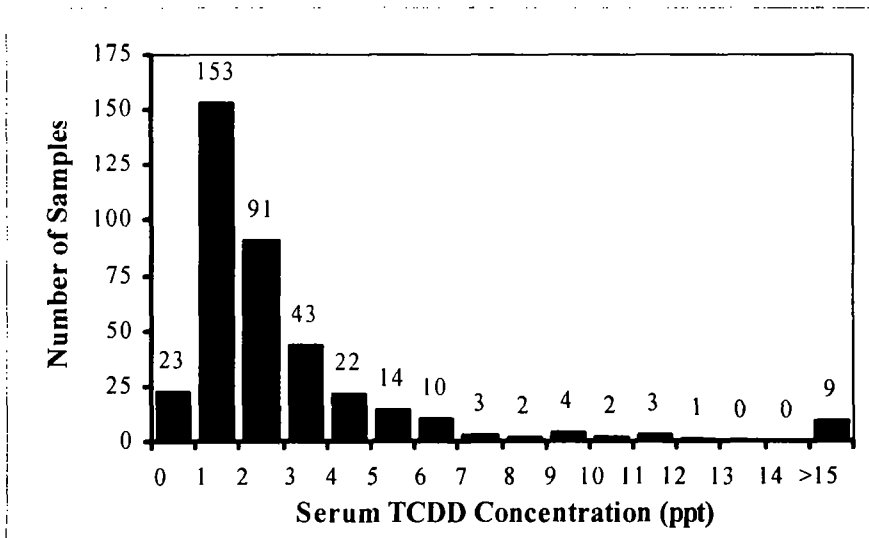
Concentrations of 2,3,7,8-TCDD were not corrected to account for (slightly different) decay times in any of the analyses. This is a simplifying assumption; the lack of individual correction is justified by the narrow time period during which the cohort reported last service (and presumed exposure) in Vietnam. The average date of last service in Vietnam was 1969; dates ranged from 1965 to 1972. The mean follow-up time between last exposure in Vietnam and blood drawing was 28 years, ranging from 26 to 33 years. These differences are slight and insignificant when compared to the reported biological half-life of dioxin (7-12 years).⁴

Finally, all exposure analyses were conducted blindly with respect to all reported health outcomes.

Results and Discussion

The distribution of serum TCDD concentrations for all members of the study group is presented as Figure 1. As expected, the concentrations were log-normally distributed with a strong skew to the right.

Figure 1: Distribution of lipid-corrected serum 2,3,7,8-TCDD concentrations in cohort (n = 380)



Preliminary analyses¹ indicated that a high degree of specificity relating to job title and herbicide-related activities was needed to accurately define potential exposure and to minimize exposure misclassification. For this reason, veterans were classified according to their questionnaire responses as having personally sprayed or otherwise handled herbicides during their military service (sprayers), having handled but not sprayed herbicides (handlers), or never personally sprayed or otherwise handled herbicides (none). Veterans were further divided by their reported service in Vietnam. Mean serum 2,3,7,8-TCDD concentrations for each of these 6 groups are reported in Table 1.

Table 1: Number of persons and mean lipid-corrected serum 2,3,7,8-TCDD concentration by service in Vietnam and self-reported history of herbicide use

		Self-reported herbicide use in military		
		Sprayer	Handler	None
Vietnam service	Yes	n = 152 c = 5.01 ppt*	n = 44 c = 2.61 ppt	n = 132 c = 2.41
	No	n = 3 c = 2.27 ppt	n = 5 c = 1.89 ppt	n = 44 c = 2.24 ppt

* where c = antilog (mean of log lipid-corrected 2,3,7,8-TCDD concentration); expressed in parts per trillion (ppt)

Examination of the data presented in Table 1 indicates that the average serum TCDD concentration for each category of herbicide use by veterans serving in Vietnam was higher than that for the corresponding category in veterans who did not serve in Vietnam, suggesting that Vietnam service may be associated with currently elevated serum TCDD concentrations. A t-test between the non-sprayers (handler + none) of persons serving in Vietnam vs. persons not serving in Vietnam was non-significant ($p = .26$).

The serum TCDD concentration for both Vietnam non-sprayer categories and all non-Vietnam herbicide use categories was approximately half that of the Vietnam sprayer category. An analysis of variance confirmed that the current serum TCDD concentrations for Vietnam sprayers were significantly higher than the remaining categories ($p = .0001$)

Additional analyses were conducted on the full study cohort in an attempt to establish an exposure-response relationship. For these analyses, measures of the frequency and duration of herbicide spraying and/or handling were abstracted from the questionnaire responses and analyzed with respect to measured serum TCDD concentrations. Cumulative herbicide exposures were estimated from responses to questions about the frequency (days per month) and duration (mean hours per day). Initially, Vietnam service, sprayer status, and the summary measures of exposure (hours of spraying and/or hours of handling) were modeled along with serum TCDD concentrations using Forward Stepwise Regression procedures. The following model resulted:

$$\log(\text{serum TCDD}) = 1.13690 + 0.13729 * \text{Vietnam} + .26912 * \text{sprayer} + .00011 * \text{hrs of exposure}$$

where: $p = .2090$ for Vietnam; $.002$ for sprayer; $.0343$ for hours of exposure

Since service in Vietnam did not contribute significantly to the model, it was dropped. A relatively simple model emerged from subsequent analysis:

$$\log(\text{serum TCDD}) = .70463 + .29621 * \text{sprayer} + .00011 * \text{hrs of exposure}$$

where: $p = .00$ for sprayer; $.032$ for hours of exposure

These analyses reinforce the observation from the unadjusted data that direct contact with herbicide as a part of spraying observations was the greatest contributor to current serum TCDD concentrations. In these analyses neither handling of herbicides or presence in Vietnam were a significant predictor of current serum TCDD concentrations.

The possible influence on serum TCDD concentrations of non-Vietnam TCDD exposure related to selected occupations was also investigated as a part of these models. While not a statistically significant contributor to any model, presumably because of the low number of samples, it should be noted that of the 7 serum TCDD concentrations >LOD in the non-Vietnam service personnel reporting no military herbicide use, 3 persons reported recent employment in the landscape and/or chemical industries.

Conclusions

By limiting analyses to subgroups of the population with the highest probability of exposure and with the lowest probability of exposure, a statistically significant difference in current serum concentrations of 2,3,7,8-TCDD was detected. Comparison of these subgroups is justified, and even preferred, as it minimizes exposure misclassification to the greatest extent possible. Regression analyses indicated that elevated concentrations of serum 2,3,7,8-TCDD were limited to actual sprayers in Vietnam and was a function of the hours sprayed. These risks were independent and statistically significant.

References

1. Kang H.K., Dalager N.A., Needham L.L., Patterson D.G., Matanoski G.M., Kanchanaraksa S., Lees P.S.J.. In Press. *Chemosphere*.
2. Dalager N.A., Kang, H.K. (1997) *Am J Ind Med* 31, 719-72 .
3. Patterson DG., Hampton L., Lapeza C.R. Jr., Belser W.T., Green V., Alexander L., Needham L.L. (1987) *Anal Chem.* 59, 2000-2005.
4. Michalek J.E., Tripathi R.C. (1999) *J Toxicol Environ Health Part A.* 57, 3 9-378.