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## SOME NOTES ON EXPOSURE TO AGENT ORANGE IN VIETNAM

Following complaints that veterans were suffering severe health problems as a result of their having been exposed to the defoliant known as Agent Orange while in Vietnam, the U.S. Congress mandated the Veterans Administration to conduct a scientific study of Vietnam veterans in order to determine what health problems may have been caused by such exposure.

The knowledge that defoliation in Vietnam was extensively used in contested areas, plus anecdotal information offered by veterans and others, suggested that most combat veterans had spent a large proportion of their Vietnam sojourn in heavily sprayed areas. A logical epidemiological study design would compare the health of a group of combat veterans who may have been exposed to significant levels of Agent Orange and its contaminant 2,3,7,8-TCDD with that of a group of similar veterans who had not had an opportunity for such exposure. Since the average person cannot accurately identify the various chemicals which they come into contact with by organoleptic means, and to avoid bias in the study, good scientific practice dictated that the assignment of veterans to high and low exposure categories for the purpose of the study must be based on documented information.

When it became known that there existed daily records of U.S. Army troop locations, as well as comparable location data for herbicide applications, it seemed feasible to match these records up on a daily basis in order to identify a cohort of men who had often been in close proximity to Agent Orange at the time of or soon after it had been sprayed, and a cohort of men who had not had any such opportunities for exposure. Preliminary work by the U.S. Army and Joint Services Environmental Support Group (ESG) indicated that the method was indeed feasible, and, although no reliable quantitative estimate of individual opportunities for exposure was available, the method was adopted by the Centers for Disease Control (CDC) as the means by which study subjects would be selected and the protocol was approved by several review groups contingent on an acceptable exposure assessment.

Futhermore, since it was anticipated that there may be some difficulty in identifying enough unexposed combat troops, a third cohort of non-combat troops who were known to have only been in areas where no herbicide spraying had been conducted were included in the study design as another unexposed comparison group.

It was unknown when the protocol was approved whether high and low exposed cohorts with significantly different exposure levels could be identified by the proposed untested methods. Following its review of the original protocol in August, 1983, the Science Panel of the Agent Orange Working Group strongly recommended a reevaluation of the cohort selection process at the end of the pilot phase of the study to assess whether "the identified high and low exposure cohorts [were] sufficiently different in exposure to Agent Orange and similar in other respects .... to make a scientifically meaningful interpretation of health outcomes." The revised protocol of November, 1983, stated that pilot study assessments would be used to make a final decision on this issue.

The investigators at CDC considered several options for assigning exposure index values to persons who may have come in contact with herbicide based on experimental data concerning the dispersion and persistence of TCDD following aerial spraying of Agent Orange. The values vary according to the time and distance from the point of herbicide application, and the expected half-life of dioxin on foliage, near the ground or in the soil. An appealing model, which assumes a half-life of about 2 days, would assign a value of one to an encounter within 24 hours of an application and decreasing values on each of the next few subsequent days. Since dispersion is thought to have been quite limited under the spray conditions which prevailed in Vietnam, a meaningful exposure was probably not possible at more than one kilometer from the point of release of the chemicals. Some digit preference and expected inaccuracies in reporting locations, plus troop dispersion, suggest that a distance greater than one kilometer will be necessary to assure that all troops who were possibly exposed receive some value on their index at each encounter.

Unfortunately, however, this will introduce missclassification in that not every score will imply a real possibility for exposure. The greater the extra distance, the larger the chance for persons with low exposure scores to have had no real opportunity for exposure at all.

The investigators at CDC have suggested 2 and 5 KM as reasonable alternatives to cover uncertainties of recorded locations. They have assembled scores for nearly 2000 combat veterans who served in III Corps during 1967 and 1968 -- a heavily contested area including Saigon and one in which considerable Agent Orange spraying occurred. The distribution of percentages of infantry, artillery, and cavalry veterans with various exposure scores at both distances and using two exposure models has been excerpted from their reports and is given below:

Exposure Score*	<u>Encounters Within</u> <u>2 Kilometers</u>		<u>Encounters Within</u> <u>5 Kilometers</u>	
	<u>E<sub>1</sub></u>	<u>E<sub>2</sub></u>	<u>E<sub>1</sub></u>	<u>E<sub>2</sub></u>
0 - .9	77.0	76.0	58.0	50.0
1 - 2.9	12.0	12.0	23.0	14.0
3 - 4.9	8.5	8.5	9.5	11.0
5 +	<u>2.5</u>	<u>3.5</u>	<u>9.5</u>	<u>25.0</u>
	100.0%	100.0%	100.0%	100.0%

\* E<sub>1</sub> = Exposure Model 1 - assigns a score of 1 to encounters on the day of spraying and 0 otherwise.

E<sub>2</sub> = Exposure Model 2 - assigns a score of 1 to encounters on the day of spraying, and lesser values on each of the next few subsequent days.

On the average, daily troop locations were known for about half of the days for the two year period from which these data were generated. When these informational "gaps" have been filled in, final scores will be higher, but almost certainly not twice as high. Many "gaps" were induced by companies' temporary relocation back to base camp positions where encounters with Ranch Hand spraying missions were unlikely, although encounters with perimeter sprayings may have occurred.

As is evident from these preliminary data, it will not be possible to identify a large number of highly exposed combat veterans. The investigators at CDC propose to change their original plan for analysis (i.e., a comparison of high and low exposure groups) to one employing logistic regression techniques in a single cohort to include all combat veteran study subjects. The analysis would estimate relative risks for health outcomes of interest along the entire range of exposure scores. Furthermore, it should have good statistical power to detect small differences in health outcomes between veterans with exposure scores of 3 to 4 versus those with scores of zero. In addition, since there appears to be an adequate number of combat veterans with essentially no opportunity for exposure, the investigators plan to de-emphasize the role of the third non-combat cohort as a back-up non-Agent Orange-exposed comparison group and utilize them as a control for measuring the health effects of combat experience.