

# Impact of Agent Orange Exposure among Korean Vietnam Veterans

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**Abstract:** In order to determine whether Agent Orange exposure was associated with increased frequency of medical problems, we conducted a cross-sectional epidemiologic study of Korean veterans during 1995–1996. 1,224 Vietnam and 154 non-Vietnam veterans were included in the study. Exposure to Agent Orange was assessed by structured in-depth interview on the participants' history of service in Vietnam. Health outcomes were assessed by a standardized comprehensive clinical investigation by a group of clinical specialists. The differences in the prevalence of various medical diagnoses were assessed by Cochran-Mantel-Haenszel chi-square tests comparing the exposure levels of Vietnam veterans, adjusting for age. Multiple logistic regression was performed to estimate the effect of "service in Vietnam" adjusting for age, smoking, alcohol, body mass index, education, and marital status. Vietnam veterans had an increased frequency of eczema (odds ratio [OR]=6.54), radiculopathy (OR=3.98), diabetes (OR=2.69), peripheral neuropathy (OR=2.39), and hypertension (OR=2.29), compared to non-Vietnam veterans, adjusting for potential confounders. In addition, higher levels of exposure among Vietnam veterans were associated with increased frequency of ischemic heart disease ( $p<0.01$ ), valvular heart disease ( $p<0.01$ ), and retinopathy ( $p<0.01$ ). We conclude that exposure to Agent Orange is associated with various health impacts in Korean Vietnam veterans.

**Key words:** Agent Orange, Dioxin, Eczema, Radiculopathy, Vietnam veterans, Korea

## Introduction

The first Korean military forces to enter South Vietnam were in the form of a Survey Team which departed for Vietnam on 19 August 1964. The last Korean units were out of South Vietnam by 23 March 1973. Korean military personnel who served in this period are about 320,000.

From 1965 to 1970, the US Air Force sprayed more than 40 million liters of Agent Orange in South Vietnam<sup>1</sup>. An additional quantity (1.6 million gallons) of herbicides was

applied to base perimeters, roadways, and communication lines by helicopter and surface sprayings from riverboats, trucks, or backpacks. Phenoxyherbicides used in Vietnam contained 1–50 ppm of the contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), also known as dioxin<sup>1</sup>. After years of concern among veterans regarding the possible long-term health consequences of exposure to phenoxyherbicides used in Vietnam and to their contaminant TCDD, several nations including USA enacted the public Law for compensations.

In Korea, after a series of appeals and demonstration by the Korean veterans demanding medical care and

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compensation for their serious health damages, a bill of medical care and compensation for herbicides victims was promulgated in March 1993 and become effective from May 1993. It is important to examine the nature and extent of the health impacts of Korean Vietnam veterans exposed to herbicides.

The long-term health consequences of exposure to phenoxyherbicides used in Vietnam have been a great concern to Korean Vietnam veterans. The purpose of this study is to identify diseases with excess prevalence compared to non-exposed veterans, with inference that the excess prevalence may indicate the health impacts of Agent Orange. The categorization of the exposure level was validated by serum TCDD measurements<sup>2)</sup>.

## Methods

### *Study population*

Since very few Korean women were sent to Vietnam, our study included only male veterans. As of March 1995, the Korean Ministry of Patriots and Veterans Affairs (MPVA) had a roster of 4,432 Vietnam male veterans who had been enrolled for health checkup. We sent a mail to invite them to the epidemiologic study. A total of 1,514 (34.2%) Vietnam veterans participated in the study. We restricted the analysis to subjects aged 45–64, who completed interview and detailed clinical investigations. This left 1,224 (27.6%) Vietnam veterans in the study.

MPVA maintained files of 32,839 non-Vietnam male veterans for pension. We identified 2,682 of them living in the vicinity of Seoul city, where the study center is located. They were mailed to invite into the study, and 154 (5.7%) non-Vietnam veterans agreed to participate in the study.

### *Data collection*

For each study participant, a standardized questionnaire was administered by a trained interviewer. Included were the questions about age, timing and duration of their service in Vietnam, their ranks and the name of troops they belonged. In addition, detailed aspects of contact with Agent Orange were asked, such as direct contacts or spray experience, drinking contaminated water, and swimming in sprayed area. Military records were obtained to complement the participants' self-reported service history.

### *Assessment of Agent Orange exposure*

The exposure assessment methodology in our study has been published elsewhere<sup>2)</sup>. However, we describe the procedure here to some details. Overall, Vietnam veterans'

exposure to Agent Orange was estimated by 4 ordered categories according to three stages. Firstly, the amount of total cumulative area exposure was estimated for each individual for his whole duration of service. Secondly, personal exposure score was constructed based on self-reported extent and frequency of contacts with Agent Orange. Finally, net exposure index was calculated by multiplying the total cumulative exposure by personal exposure score, and then categorized into quartiles to represent the level of the individual's exposure.

In the first stage, estimation of the cumulative area exposure again involved three steps. First, all the areas of Vietnam were divided into 4 military regions, and for each region the information on the annually sprayed amount of Agent Orange was obtained from military data. Second, individual study participant's relative exposure for each year was calculated by multiplying the amount of Agent Orange sprayed in his service locations by his service durations for each location in the year. Third, the participant's yearly exposure was summed up for the whole service period, including multiple services in different occasions. This procedure lead to a service-exposure matrix resulting in a relative index of cumulative area exposure for each individuals. This index reflects the total amount of Agent Orange sprayed during the veteran's service in the military region where he served.

Since the total cumulative area exposure did not reflect individual variations in contact experiences with the sprayed Agent Orange, we developed a scoring system to indicate the intensity of personal exposure during his service. The scoring involved a weight for the type of contact and another for the frequency. In the questionnaire interview, we obtained the information on the type of the exposure episodes, such as dermal contact to Agent Orange (weight=1.4), direct exposure to sprayed Agent Orange (1.2), intentional spray by himself to avoid insect bites, and exposure to contaminated water by drinking or swimming (1.0). The frequency of exposure episodes per whole service was grouped into six categories: none, 1–3, 4–7, 8–11, 14–30, and over 30 based on distribution among the study population. Weights were given to the frequency categories as 1/6, 2/6, 3/6, 4/6, 5/6, and 1. Non-Vietnam veterans were given zero weights for the frequency. In order to reflect all types of exposure episodes, the two weights for the type and frequency of exposure episodes were multiplied respectively and then summed over all types. This sum ranged from 0 to 5.8 among our study participants. Personal exposure score was calculated by dividing the individual sum of weights by the maximum value 5.8. Therefore, this score ranges from 0 to

1, and implies the ratio of the intensity of a person's exposure to the maximum intensity in our population.

In the third stage, the total cumulative exposure was multiplied by the personal exposure score, resulting in the net exposure index. This index reflects the total amount of sprayed Agent Orange in a person's service areas over the whole service period, as well as the individual variation via different routes of exposure. Eventually, the index was categorized into quartiles, so that the Vietnam veterans' exposure levels were grouped into four ordered categories.

#### *Validation of exposure assessment*

TCDD accumulates preferentially in the body fat, and the median half-life of TCDD estimated from Air Force personnel involved in the Operation Ranch Hand spraying mission in Vietnam was 7.6 years with 95% confidence interval 7.0 to 8.2 years<sup>3</sup>). These data indicated that it should be possible to detect elevated levels of TCDD in persons even many years after their exposure if they were exposed to a substantial amount of TCDD. Also many studies imply that TCDD levels in human biological specimens could serve as a marker of exposure to Agent Orange<sup>3, 4</sup>).

In an effort to validate our method of exposure assessment based on interview, we measured TCDD in the stored blood samples drawn at the time of health examination. The procedure has been described in detail<sup>2</sup>). Since the stored blood samples were typically less than 1 ml per subject, we had to construct pooled samples for the chemical analyses. We randomly selected 745 samples in total, including 25 from non-Vietnam veterans and 180 from each of the four exposure groups among Vietnam veterans.

One pooled sample for non-Vietnam veterans and 3 pooled samples for each of the exposure categories were prepared, resulting in 13 pooled sample sets. These samples were sent to CDC and analyzed according to the standard protocol<sup>5</sup>). The lipid adjusted values of TCDD levels from the 13 pooled samples ranged from 0.25 to 1.2 pg/g, with a median of 0.7 and a mean of 0.68 pg/g.

The mean values of TCDD levels for the five exposure categories were 0.3, 0.6, 0.62, 0.78, 0.87 pg/g, respectively. Because of our small sample size, our data did not show a significant linear correlation with the ordinal exposure categories. However, the distinct monotone upward trend gave us some confidence in the validity of our approach to exposure assessment.

#### *Assessment of health outcomes*

Our approach to assessment of health outcomes can be characterized as "standardized comprehensive clinical

investigation" by a group of clinical specialists. This was because the purpose of the assessment included decision-making for compensation if a participant meets the criteria for medical problems known or newly determined to be associated with Agent Orange exposure. Four family medicine specialists examined the participants thoroughly and screened them for further referral to other specialists. The assessment focused on six major clinical areas: endocrinology, neurology, psychiatry, dermatology, cardiovascular medicine, and ophthalmology, each with two specialists involved. Clinical specialists in each area developed a standardized clinical protocol including full investigations such as symptom questionnaire, clinical interview, physical examination, blood tests, Chest X-ray, electrocardiograph, and special tests including computerized tomography (CT), magnetic resonance imaging, nerve conduction velocity (NCV), electromyography, Doppler vascular imaging and biopsy, as needed according to standard clinical indications. All assessment procedures were performed without the information on individuals' exposure status. As a means of quality assurance, we sent a random sample of X-ray films and NCV recordings to outside specialists. Kappa agreement indices were 0.89, 0.63, 0.56, and 0.39, for brain CT, Chest X-ray, NCV, and vertebral CT, respectively.

#### *Statistical analysis*

Health outcomes were classified by ICD-9 system within each of the clinical areas we studied. We compared the frequency of health outcomes among the exposure categories in three ways. First, the frequency of the outcome was compared across all the exposure categories, including non-Vietnam veterans as well as Vietnam veterans with four exposure levels. Second, comparison was made within Vietnam veterans across the exposure levels. Third, the frequency of the outcome was compared between Vietnam and non-Vietnam veterans. For all comparisons, generalized Cochran-Mantel-Haenszel chi-square tests were performed adjusting for age, in order to assess whether there is association between the frequency of the outcome and the exposure status<sup>6</sup>). For the outcomes that showed significant association in the stratified analyses, multiple logistic regression analyses were performed to assess the effect of exposure status adjusting for age, smoking, alcohol, body mass index (BMI), education, and marital status.

## **Results**

To assess the possibility of selection bias, general characteristics were compared between participants and non-

**Table 1. Characteristics of study participants and nonparticipants among Vietnam veterans who had received health examination in the Korean Ministry of Patriots and Veterans Affairs (N=4,432)**

Variables	Participants (N=1,224)		Nonparticipants (N=3,208)	
	N	(%)	N	(%)
Age (yr)				
40–44	0	(0.0)	59	(1.9)
45–49	422	(34.5)	1,503	(47.1)
50–54	673	(55.0)	1,303	(40.8)
55–59	85	(6.9)	188	(5.9)
60–64	44	(3.6)	138	(4.3)
Year of dispatch				
63–66	401	(32.8)	641	(22.4)
67–69	682	(55.7)	1,235	(43.2)
70–71	141	(11.5)	755	(26.4)
≥ 72	0	(0.0)	229	(8.0)
Service duration (months)				
≤ 6	35	(2.9)	106	(3.7)
7–12	505	(41.3)	1,297	(45.7)
13–18	472	(38.6)	966	(34.1)
19–25	142	(11.6)	272	(9.6)
26–35	61	(5.0)	162	(5.7)
≥ 36	9	(0.7)	34	(1.2)
Military region				
I	73	(6.0)	372	(14.2)
II	1,116	(91.2)	2,200	(83.9)
III	35	(2.9)	49	(1.9)

participants among Vietnam veterans enrolled in MPVA (Table 1). Compared to nonparticipants, participants tended to be in the older group, have served in Vietnam earlier and longer.

The groups with different exposure status were compared for general characteristics (Table 2, 3). Some subjects did not give sufficient information for certain variables; this led to fewer numbers of subjects than the column total for military rank and education in Table 2, and smoking amount and alcohol amount in Table 3. In general, non-Vietnam veterans appear to be different from Vietnam veterans in several aspects. The former group is older, mostly married, lower in the military rank, and higher in education compared to the latter. However, there was no significant difference in health insurance status, which is a marker for socioeconomic position. Among Vietnam veterans, the lowest exposure group was relatively younger and slightly higher in education, but similar to other exposure groups in the other aspects. Mean BMI were not significantly different. Smoking and alcohol drinking amount was higher in non-Vietnam veterans.

Table 4 shows the frequency of endocrinologic and neurologic diseases by exposure groups. Several disease

categories showed a significant difference in the frequency between Vietnam and non-Vietnam veterans. They are diabetes mellitus ( $p=0.02$ ), peripheral neuropathy ( $p=0.004$ ), radiculopathy including herniation of nucleus pulposus ( $p<0.001$ ), brain atrophy ( $p=0.02$ ) and brain infarction ( $p=0.001$ ). However, none of these outcomes were significantly associated with the exposure levels within Vietnam veterans.

In Table 5, psychiatric and dermatologic diagnoses were compared among groups. Mood disorder, post-traumatic stress disorder, and eczema were significantly more frequent in Vietnam veterans compared to non-Vietnam veterans ( $p<0.05$ ). Again, none of these showed significant difference across exposure levels within Vietnam veterans.

Cardiovascular, ophthalmologic, and other health outcomes are shown in Table 5. Compared to non-Vietnam veterans, Vietnam veterans had significantly higher frequency of hypertension, vasculopathy, valvular heart disease, uroporphyrinuria, and cell function markers such as plating efficiency and mitogen response. When the association of the outcomes across all exposure strata was assessed, retinopathy, anemia, and coproporphyrinuria were also

**Table 2. General characteristics of study participants by Agent Orange exposure status (N=1,224)**

Variable	Non-Vietnam veterans (N=154)	Vietnam veterans				p-values for difference <sup>1)</sup>		
		Level 1 (N=307)	Level 2 (N=305)	Level 3 (N=306)	Level 4 (N=306)	Among all categories	Among categories of Vietnam veterans	Between non-Vietnam vs. all Vietnam veterans
Age (yr)								
45–49	47 (30.5)	157 (51.1)	78 (25.6)	94 (30.7)	93 (30.4)			
50–54	51 (33.1)	121 (39.4)	191 (62.6)	172 (56.2)	189 (61.8)	<0.01	<0.01	<0.01
55–59	3 (2.0)	18 (5.9)	19 (6.2)	30 (9.8)	18 (5.9)			
60–64	53 (34.4)	11 (3.6)	17 (17.5)	10 (3.3)	6 (2.0)			
Married	151 (98.1)	276 (89.9)	288 (94.4)	276 (90.2)	276 (90.2)	0.35	0.53	0.01
Health insurance								
Insured	119 (78.3)	253 (81.9)	242 (81.2)	240 (79.7)	238 (79.3)	0.27	0.09	0.68
Medical aid	33 (21.7)	56 (18.1)	56 (18.8)	61 (20.3)	62 (20.7)			
Military rank								
Soldier	154 (100)	229 (78.4)	224 (77.2)	232 (80.5)	235 (81.0)	0.15	0.15	<0.01
Officer	0 (0)	63 (21.6)	66 (21.8)	56 (19.5)	55 (19.0)			
Education								
Primary school or lower	27 (17.7)	96 (31.5)	120 (39.5)	141 (46.6)	113 (37.4)			
Middle school	54 (35.3)	106 (34.8)	99 (32.6)	81 (26.7)	99 (32.8)	<0.01	0.05	<0.01
High school or above	72 (47.1)	103 (33.7)	85 (27.9)	81 (26.7)	90 (29.8)			

<sup>1)</sup> Obtained by Cochran-Mantel Haenszel Chi-Square test.

**Table 3. Behavioral risk factors of study participants by Agent Orange exposure status (N=1,224)**

Variable	Non-Vietnam veterans (N=154)	Vietnam veterans				p-values for difference <sup>1)</sup>		
		Level 1 (N=307)	Level 2 (N=305)	Level 3 (N=306)	Level 4 (N=306)	Among all categories	Among categories of Vietnam veterans	Between non-Vietnam vs. all Vietnam veterans
BMI (mean, SD)	24.1 (2.9)	23.7 (3.1)	23.7 (3.3)	23.7 (3.1)	23.9 (3.1)	0.36	0.42	0.19
Smoking amount <sup>2)</sup> (cigaretts/year)								
0	28 (19.7)	76 (29.3)	74 (29.7)	82 (34.0)	74 (33.2)	<0.01	0.73	<0.01
0–112	5 (3.5)	32 (12.4)	33 (13.3)	26 (10.8)	27 (12.1)			
112–6,043	82 (57.8)	143 (55.2)	128 (51.4)	117 (48.6)	116 (52.0)			
≥ 6,044	27 (19.0)	8 (3.1)	14 (5.6)	16 (6.6)	6 (2.7)			
Alcohol amount ever drunk <sup>2)</sup> (in bottles of liquor <sup>3)</sup> unit)								
0	29 (24.2)	113 (49.1)	109 (48.0)	114 (48.1)	99 (46.9)	<0.01	0.99	<0.01
0–316	6 (5.0)	15 (6.5)	22 (9.7)	16 (6.8)	26 (12.3)			
317–4,446	60 (50.0)	89 (38.7)	83 (36.6)	92 (38.8)	69 (32.7)			
≥ 4,447	25 (20.8)	13 (5.7)	13 (5.7)	15 (6.3)	17 (8.1)			

<sup>1)</sup> Obtained by Cochran-Mantel Haenszel Chi-Square test adjusting for age. <sup>2)</sup> Categorized by the cutoffs for the highest and the lowest 15 percentiles among all subjects. <sup>3)</sup> One bottle of Korean liquor (“So-Ju”) includes 72 grams of alcohol.

statistically significant ( $p < 0.05$ ). Within Vietnam veterans, ischemic heart disease, valvular heart disease, and retinopathy were significantly associated with exposure levels.

Results from multiple logistic regression analysis are shown in Table 7. In addition to age, other variables such as alcohol, smoking, BMI, education and marital status were

adjusted. In general, the results were consistent with the results from stratified analyses. Eczema showed a strongest association with Vietnam veterans compared to non-Vietnam veterans, and radiculopathy had the next strongest association, followed by diabetes mellitus, peripheral neuropathy, and hypertension.

**Table 4. Number and percentage of endocrinologic and neurologic diagnoses by Agent Orange exposure status**

Variable	Non-Vietnam veterans (N=154)	Vietnam veterans				p-values for difference <sup>1)</sup>		
		Level 1 (N=307)	Level 2 (N=305)	Level 3 (N=306)	Level 4 (N=306)	Among all categories	Among categories of Vietnam veterans	Between non-Vietnam vs. all Vietnam veterans
<b>Endocrinologic</b>								
Diabetes mellitus	9 (5.8)	37 (12.1)	35 (11.5)	39 (12.8)	43 (14.1)	0.1811	0.7844	0.0230
Hyperthyroidism	0 (0.0)	2 (0.7)	3 (1.0)	2 (0.7)	2 (0.7)	0.8582	0.9295	0.3625
Hypothyroidism	1 (0.7)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	0.3893	0.5816	0.1064
<b>Neurologic</b>								
Neuropathy with DM	1 (0.7)	6 (2.0)	4 (1.3)	5 (1.6)	6 (2.0)	0.7147	0.8838	0.2157
Mononeuropathy	2 (1.3)	6 (2.0)	5 (1.6)	1 (0.3)	2 (0.7)	0.3211	0.2184	0.8573
Peripheral neuropathy	5 (3.3)	33 (10.8)	43 (14.1)	42 (13.7)	32 (10.5)	0.0211	0.3914	0.0042
Radiculopathy including HIVD	23 (14.9)	117 (38.1)	114 (37.4)	119 (38.9)	128 (41.8)	<0.0001	0.6863	<0.0001
Radiculopathy	19 (12.3)	93 (30.3)	86 (28.2)	79 (25.8)	94 (30.7)	0.0039	0.5980	0.0002
Herniation of nucleus pulposus	7 (4.6)	32 (10.4)	34 (11.2)	49 (16.0)	44 (14.4)	0.0069	0.1661	0.0028
Myelopathy	1 (0.7)	6 (2.0)	6 (2.0)	11 (3.6)	12 (3.9)	0.0874	0.1968	0.0851
Motor neuron disease	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.7)	2 (0.7)	0.6495	0.5818	0.5406
Spondylosis	0 (0.0)	5 (1.6)	5 (1.6)	4 (1.3)	3 (1.0)	0.5504	0.8814	0.1311
Parkinson's disease	0 (0.0)	2 (0.7)	2 (0.7)	4 (1.3)	3 (1.0)	0.5915	0.8165	0.1830
Brain atrophy except cerebellum	0 (0.0)	4 (1.3)	7 (2.3)	9 (2.9)	3 (1.0)	0.0455	0.3365	0.0165
Brain infarction	1 (0.7)	19 (6.2)	16 (5.3)	22 (7.2)	18 (5.9)	0.0193	0.7254	0.0013
Intracranial hemorrhage	1 (0.7)	3 (1.0)	1 (0.3)	1 (0.3)	0 (0.0)	0.4362	0.2823	0.9577
Epilepsy	0 (0.0)	4 (1.3)	2 (0.7)	4 (1.3)	1 (0.3)	0.4990	0.5578	0.2956

<sup>1)</sup> Obtained by Cochran-Mantel Haenszel Chi-Square test adjusting for age. DM: diabetes mellitus, HIVD: herniated intervertebral disc.

## Discussion

In our cross-sectional study of Korean veterans, we found that Vietnam veterans had higher frequency of numerous clinical diseases compared to non-Vietnam veterans. However, most of them were not associated with our estimation of the Agent Orange exposure status within Vietnam veterans. Frequency of certain diseases such as ischemic heart disease, valvular heart disease, and retinopathy were associated with exposure levels within Vietnam veterans. This discrepancy may indicate either overestimation of certain disease frequencies among Vietnam veterans, underestimation of the association with exposures, or both.

Several aspects in our study need to be considered in order to interpret our results. First, our study population covered only a fraction of complete cohort of Vietnam and non-Vietnam veterans, because complete identification was not possible in any way. Our study targeted the Vietnam veterans who volunteered to contact MPVA to receive a health check-up to get any sort of compensation. In addition, as a comparison group, we targeted the non-Vietnam veterans who had been receiving pension regularly from MPVA. Among those target population, we included those who responded to our mail invitation to the study. If the study

was understood as a possibility for new or additional compensation, it is reasonable to speculate that Vietnam veterans might have had higher motivation to participate, especially if they had been experiencing symptomatic medical problems. Selection bias is less likely for internal comparison within Vietnam veterans across the exposure status. Therefore, ischemic heart disease, valvular heart disease, and retinopathy may better reflect the effect of Agent Orange exposure among Vietnam veterans. Multiple logistic regression analysis showed that Vietnam veterans had higher frequency of several outcomes compared to non-Vietnam veterans, after adjusting for age, smoking, alcohol, education, BMI, and marital status. These procedures should have allowed us to a certain degree to avoid bias arising from self-selection of individuals with high risk profile.

The second aspect in our study is the assessment of exposure to Agent Orange among Vietnam veterans. This has been a challenge in all the studies on Vietnam veterans. We considered environmental and personal variations as well as various possible routes of exposure, with a structured interview questionnaire. However, measurement error must be present to a certain degree, and such error is expected to be largely nondifferential with regard to the health outcomes, likely resulting in an attenuation of the magnitude of

**Table 5. Number and percentage of psychiatric and dermatologic diagnoses by Agent Orange exposure status**

Exposure levels Diseases	Vietnam veterans					p-values for difference <sup>1)</sup>		
	Non-Vietnam	Level 1	Level 2	Level 3	Level 4	Among all categories	Among categories of Vietnam veterans	Between non- Vietnam vs. all Vietnam veterans
<b>Psychiatric</b>								
Anxiety disorder	0 (0.0)	2 (0.7)	5 (1.6)	7 (2.3)	3 (1.0)	0.2497	0.3078	0.2230
Schizophrenia	1 (0.7)	1 (0.3)	1 (0.3)	4 (1.3)	3 (1.0)	0.5646	0.3855	0.8084
Mood disorder	0 (0.0)	10 (3.3)	10 (3.3)	7 (2.3)	8 (2.6)	0.2238	0.8857	0.0264
Post traumatic stress disorder	1 (0.7)	21 (6.8)	27 (8.9)	28 (9.2)	30 (9.8)	0.0147	0.4682	0.0018
<b>Mental and behavioral disorders due to alcohol use</b>								
Amnesic disorder	4 (2.6)	21 (6.8)	16 (5.3)	14 (4.6)	14 (4.6)	0.5886	0.5067	0.4935
Sleep disorder	0 (0.0)	5 (1.6)	6 (2.0)	2 (0.7)	6 (2.0)	0.3700	0.5149	0.1813
<b>Dermatologic</b>								
Chloracne	0 (0.0)	4 (1.3)	2 (0.7)	1 (0.3)	2 (0.7)	0.3872	0.5492	0.1914
Acne	0 (0.0)	2 (0.7)	0 (0.0)	3 (1.0)	1 (0.3)	0.3720	0.3353	0.4529
Folliculitis	0 (0.0)	3 (1.0)	4 (1.3)	5 (1.6)	5 (1.6)	0.6634	0.8560	0.2122
Hemangioma	0 (0.0)	5 (1.6)	2 (0.7)	0 (0.0)	2 (0.7)	0.1847	0.2834	0.1777
Psoriasis	1 (0.7)	15 (4.9)	10 (3.3)	9 (2.9)	8 (2.6)	0.3249	0.4524	0.1852
Parapsoriasis	0 (0.0)	1 (0.3)	1 (0.3)	1 (0.3)	0 (0.0)	0.8692	0.8108	0.6373
Eczema	7 (4.6)	67 (21.8)	68 (22.3)	75 (24.5)	76 (23.8)	<0.0001	0.6409	<0.0001
Seborrheic dermatitis	2 (1.3)	24 (7.8)	27 (8.9)	40 (13.1)	32 (9.2)	0.0009	0.1194	0.0004
Xerotic eczema	2 (1.3)	13 (4.2)	23 (7.5)	19 (6.2)	14 (6.2)	0.0798	0.2867	0.0385
Neurodermatitis	2 (1.3)	20 (6.5)	22 (7.2)	16 (5.2)	24 (7.3)	0.0607	0.6364	0.0073
Photosensitive dermatitis	0 (0.0)	7 (2.3)	6 (2.0)	3 (1.0)	6 (4.4)	0.2849	0.5283	0.1082
Pruritus	1 (0.7)	10 (3.3)	7 (2.3)	11 (3.6)	12 (0.0)	0.2650	0.5742	0.0739
Telangiectasis	0 (0.0)	2 (0.7)	3 (1.0)	4 (1.3)	2 (0.0)	0.5869	0.8265	0.1788
Prurigo	0 (0.0)	3 (1.0)	8 (2.6)	5 (1.6)	3 (1.5)	0.1677	0.3190	0.1163
Vitiligo	1 (0.7)	4 (1.3)	3 (1.0)	1 (0.3)	1 (0.7)	0.5062	0.3554	0.7771
Verucca	0 (0.0)	1 (0.3)	1 (0.3)	1 (0.3)	3 (1.1)	0.5694	0.5095	0.5042
Alopecia	1 (0.7)	2 (0.7)	2 (0.7)	3 (1.0)	4 (1.1)	0.9291	0.8464	0.9697
Urticaria	0 (0.0)	8 (2.6)	8 (2.6)	9 (2.9)	7 (2.2)	0.4545	0.9869	0.0614
Keratoderma	0 (0.0)	3 (1.0)	2 (0.7)	3 (1.0)	1 (0.0)	0.6317	0.6421	0.3839
Post inflammatory hyperpigmentation	0 (0.0)	1 (0.3)	4 (1.3)	2 (0.7)	2 (0.7)	0.4959	0.4778	0.3991

<sup>1)</sup> Obtained by Cochran-Mantel Haenszel Chi-Square test adjusting for age.

association. Therefore, lack of association between our estimated exposure levels and some of the diseases more frequent in Vietnam veterans might have been due to imprecise measurement of exposure. On the other hand, there is some possibility that the subjects over-reported their personal episodes of exposure if they have health problems, leading to a recall bias. Our exposure assessment interview was performed based on a structured questionnaire to minimize this problem. Increasing trend of measured TCDD levels in association with the exposure categories suggests that the recall bias would not have dominated our results.

In general, TCDD measurements in our study participants appear to be lower than those in the past studies. However the amount of TCDD measured showed a tendency of dose-

response relationship with the level of exposure we classified although statistically non-significant, owing to the small sample size<sup>2)</sup>. It is not clear whether this implies that Korean veterans were less exposed to Agent Orange. TCDD levels may have been reduced because of time lag, or there may be differences in metabolism among ethnic groups. With many reports of direct contact episodes with Agent Orange in our Vietnam veterans, we consider it less likely that Korean veterans had particularly lower exposure to TCDD compared to other nationals who experienced the same battles in the same regions.

The patterns of the medical problems among Vietnam veterans in our study appear to be somewhat consistent with previous reports from Operation Ranch Hand study and

**Table 6. Number and percentage of cardiovascular, ophthalmic, and other clinical diagnoses by Agent Orange exposure status**

Exposure levels Diseases	Vietnam veterans					p-values for difference <sup>1)</sup>		
	Non-Vietnam	Level 1	Level 2	Level 3	Level 4	Among all categories	Among categories of Vietnam veterans	Between non-Vietnam vs. all Vietnam veterans
<b>Cardiovascular</b>								
Hypertension	43 (27.9)	93 (30.3)	97 (31.8)	93 (30.4)	100 (32.7)	0.1602	0.9000	0.0143
Vasculopathy	0 (0.0)	21 (6.8)	22 (7.2)	24 (7.8)	31 (10.1)	0.0019	0.3777	0.0002
Arteriosclerosis	0 (0.0)	4 (1.3)	6 (2.0)	9 (2.9)	7 (2.3)	0.3155	0.5280	0.1270
Peripheral vasculopathy <sup>2)</sup>	0 (0.0)	11 (3.6)	7 (2.3)	10 (3.3)	7 (2.3)	0.3617	0.8464	0.0628
Ischemic heart disease	0 (0.0)	6 (2.0)	10 (3.3)	5 (1.6)	13 (10.1)	0.0011	0.0277	0.0045
Valvular heart disease	0 (0.0)	1 (0.3)	0 (0.0)	6 (2.0)	1 (0.3)	0.0020	0.0019	0.0019
Congestive heart failure	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.7)	2 (0.7)	0.5638	0.5109	0.5018
Varicose vein	0 (0.0)	1 (0.3)	2 (0.7)	2 (0.7)	2 (0.7)	0.7299	0.9346	0.2152
<b>Ophthalmologic</b>								
Cataract	1 (0.7)	5 (1.6)	7 (2.3)	3 (1.0)	4 (1.3)	0.6151	0.5983	0.4274
Glaucoma	0 (0.0)	4 (1.3)	1 (0.3)	3 (1.0)	2 (0.7)	0.4063	0.4032	0.3607
Exudative degeneration	0 (0.0)	4 (1.3)	3 (1.0)	2 (0.7)	1 (0.3)	0.5413	0.5696	0.3412
Retinopathy	1 (0.7)	1 (0.3)	0 (0.0)	0 (0.0)	6 (2.0)	0.0100	0.0039	0.5733
Retinopathy with diabetes mellitus	0 (0.0)	2 (0.7)	2 (0.7)	0 (0.0)	1 (0.3)	0.5860	0.5343	0.5018
Retinopathy with hypertension	0 (0.0)	1 (0.3)	2 (0.7)	4 (1.3)	3 (1.0)	0.2534	0.5239	0.0978
<b>Hematologic</b>								
Macrocytosis	9 (5.8)	10 (3.3)	11 (3.6)	10 (3.3)	9 (2.9)	0.9541	0.9828	0.4783
Pancytopenia	0 (0.0)	1 (0.3)	2 (0.7)	0 (0.0)	1 (0.3)	0.5085	0.4520	0.5213
Anemia	0 (0.0)	9 (2.9)	1 (0.3)	7 (2.3)	4 (1.3)	0.0470	0.1467	0.0571
<b>Porphyria</b>								
Uroporphyrin	9 (6.2)	55 (18.4)	63 (21.7)	57 (19.3)	71 (24.0)	<0.0001	0.1304	<0.0001
Coproporphyrin	2 (1.4)	11 (3.7)	9 (3.1)	16 (5.5)	11 (3.7)	0.0373	0.5447	0.1628
<b>Cell function</b>								
Plating efficiency	39 (68.4)	33 (44.6)	42 (60.7)	31 (47.0)	30 (47.6)	0.0226	0.2095	<0.0077
Mitogen response	20 (51.3)	7 (21.2)	11 (26.2)	4 (12.9)	7 (23.3)	0.0013	0.5492	<0.0001

<sup>1)</sup> Obtained by Cochran-Mantel Haenszel Chi-Square test adjusting for age. <sup>2)</sup> Includes Burger's disease, Raynaud's syndrome, and other vasculopathy.

**Table 7. Association between types of diseases and Agent Orange exposure status<sup>1)</sup>**

Outcomes	$\beta^2)$	OR	95% CI	p-value
Diabetes Mellitus	0.989	2.69	(1.09 6.67)	0.033
Eczema	1.878	6.54	(2.71 15.80)	<0.001
Hypertension	0.829	2.29	(1.33 3.95)	0.003
Peripheral neuropathy	0.872	2.39	(1.04 5.48)	0.039
Radiculopathy	1.382	3.98	(2.19 7.26)	<0.001

<sup>1)</sup> All Vietnam veterans are defined as the exposed group. <sup>2)</sup> Adjusted for alcohol, smoking, BMI, education, age, and marital status by multiple logistic regression analyses.

others. On the other hand, we observe an additional pattern that hypertension and ischemic heart disease were associated with exposure levels. For hypertension, we adjusted for major cardiovascular risk factors such as age, smoking, BMI, and socioeconomic position indicated by education and marital status. Therefore we consider residual confounding

would have been limited. Other cardiovascular outcomes were absent in our non-Vietnam participants. It is not clear whether this difference is truly because of Agent Orange exposure, or other unmeasured factors associated with the exposure. However, this observation needs to be considered in further investigations.



## Conclusion

We observed excess frequencies of several medical problems such as diabetes mellitus, eczema, hypertension, peripheral neuropathy, and radiculopathy, among Vietnam veterans compared to non-Vietnam veterans. The increased frequencies of these diseases remained significant even after adjusting for age, smoking, alcohol, body mass index, education, and marital status. Also increased were vasculopathy and brain infarction. In addition, ischemic heart disease, valvular heart disease, and retinopathy were significantly associated with the levels of exposure to Agent Orange, among Vietnam veterans. These findings coherently suggest that Vietnam veterans have higher frequency of vasculopathy in association with Agent Orange exposure.

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