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## Serum Dioxin and Psychological Functioning in U.S. Air Force Veterans of the Vietnam War

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Using the Minnesota Multiphasic Personality Inventory and the Millon Clinical Multiaxial Inventory, we assessed the psychological functioning of U.S. Air Force veterans exposed to Agent Orange and its contaminant, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (dioxin), during the Vietnam War. Index subjects were veterans of Operation Ranch Hand ( $N = 1,109$ ). Comparisons ( $N = 1,493$ ) were U.S. Air Force veterans not involved with spraying herbicides. We found few consistent psychological abnormalities associated with serum dioxin levels. Ranch Hand veterans with higher dioxin levels showed some difficulties in anxiety, somatization, depression, and a denial of psychological factors. However, those with background levels also showed indications of emotional distress, primarily in emotional numbing and lability; a guarded, suspicious, and withdrawn style of relating to others; and unusual thoughts or behaviors.

### Introduction

There is substantial literature documenting the psychological impact of military service in Vietnam. Vietnam veterans have been found to have a higher prevalence than their nondeployed peers of a variety of psychological problems, including alcohol abuse or dependence, anxiety, depression, and post-traumatic stress disorder.<sup>1</sup> Vietnam veterans also have more concerns about their physical health than their peers who were not deployed.<sup>2</sup> For many Vietnam veterans, this concern has focused on fear of the health impact of exposure to Agent Orange. However, the extent of herbicide and dioxin exposure for most U.S. Vietnam veterans is unknown.

Approximately 19 million gallons of herbicide, of which 11.2 million gallons were Agent Orange, were sprayed by U.S. military personnel during the Vietnam War.<sup>3</sup> Considerable research has been conducted investigating the long-term health consequences of Agent Orange and its contaminant, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (dioxin), and much of this has been periodically reviewed by the Institute of Medicine, National Academy of Sciences.<sup>3-7</sup> The Institute of Medicine has found sufficient evidence for an association between dioxin exposure and the development of soft tissue sarcoma, non-Hodgkin's lymphoma, Hodgkin's disease, and chloracne.<sup>4</sup> More recently dioxin exposure has been found to be associated with diabetes.<sup>6,8</sup>

In late 1978, Congress directed the U.S. Air Force to investigate the health status of U.S. Air Force veterans of Operation Ranch Hand, the unit responsible for the aerial spraying of

Agent Orange and other herbicides in Vietnam from 1962 to 1971. Ranch Hand veterans were exposed to herbicides during loading operations, while maintaining the aircraft and herbicide spraying equipment and while in flight. The resultant U.S. Air Force Health Study is an ongoing 20-year prospective investigation of the health,<sup>8-15</sup> mortality experience,<sup>16,17</sup> and reproductive outcomes<sup>18-21</sup> of these veterans.

The U.S. Air Force Health Study and other studies of dioxin exposure among Vietnam veterans have primarily focused on assessing physical health outcomes. Although psychological outcomes among Vietnam veterans have been studied, only a few studies have examined the association between dioxin exposure and psychological health.<sup>22,23</sup> However, these studies have been limited by reliance on self-reports of exposure or information from military records of spraying.

Previous studies examining the psychological impact of exposure to Agent Orange have had to rely on less direct exposure estimates. For example, in a study of 100 Vietnam veterans, herbicide exposure was estimated using military records giving the location of each veteran's duty station in Vietnam.<sup>22</sup> By comparing this information with computer records of herbicide spraying missions, researchers calculated a numerical estimate of the likelihood of herbicide exposure. Veterans were then classified as either exposed or unexposed based on the median of the estimated numerical exposure score. No significant differences on mean scores on the Minnesota Multiphasic Personality Inventory (MMPI)<sup>24</sup> scales were found between veterans classified as exposed and those classified as unexposed. However, significant differences were found when veterans were classified based on self-perception of exposure. Veterans who believed they were exposed scored significantly higher on all MMPI scales except scale 5 (masculinity-femininity), where there was no significant difference, and scale K (denial, defensiveness), where veterans who believed they were exposed scored significantly lower than those who were unsure about their exposure.

A study of 153 Vietnam veterans seeking treatment for substance abuse also found a relation between self-reported Agent Orange exposure and psychological functioning.<sup>23</sup> Veterans were asked "How often were you exposed to chemical defoliants such as "Agent Orange" in Vietnam?" Those who responded "occasionally," "often," or "very often" were classified as having "high" Agent Orange exposure; those who responded "rarely" or "never" were classified as having "low" Agent Orange exposure. Veterans in the high Agent Orange exposure group scored significantly higher than veterans in the low exposure group on 8 of the 13 basic MMPI scales (F, validity; 1, hypochondriasis; 2, depression; 6, paranoia; 7, psychasthenia; 8, schizophrenia; 9, hypomania; 0, social introversion); veterans classified as having high exposure scored significantly lower on scale K (denial,

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defensiveness). When the analyses were adjusted for age, education, and degree of combat experience, veterans classified as having high Agent Orange exposure continued to score significantly higher on scales F (validity), 7 (psychasthenia), and 8 (schizophrenia). The authors concluded that the psychological functioning of veterans who believe they were exposed to Agent Orange is characterized by an increased help-seeking orientation; greater vulnerability to emotional distress and depression; a tendency toward somatization; a guarded, suspicious, and withdrawn type of relating to others; and unusual thought processes. Similar results have been found for Vietnam veterans in general, where MMPI results suggested problems with anxiety, somatization, depression, and unusual thought or behavioral patterns among a large group of U.S. Army veterans.<sup>1</sup>

The purpose of this study was to assess the personality, emotional status, and level of psychopathology of Ranch Hand veterans with varying levels of dioxin exposures measured by serum testing. We tested the null hypothesis of no association between dioxin exposure and psychological functioning as measured by two self-administered questionnaires.

## Method

### U.S. Air Force Health Study Background

The details of study design and veteran selection used in the U.S. Air Force Health Study are published elsewhere.<sup>15</sup> The U.S. Air Force Health Study seeks to determine whether veterans of Operation Ranch Hand have experienced adverse health and whether any effects, if they exist, can be attributed to exposure to herbicides or their dioxin contaminant. The study compares the current health and cumulative mortality experience of Ranch Hand veterans with a comparison group of other U.S. Air Force veterans who served in Southeast Asia during the same period (1962-1971) that the Ranch Hand unit was active and who were not involved with spraying herbicides. Comparisons were matched to Ranch Hand veterans on age, race, and occupation. All Ranch Hand and comparison veterans are men. Longitudinal data have been gathered from a series of physical and psychological examinations that began in 1982.

### Psychological Assessment

Subjects were administered the MMPI<sup>24</sup> in 1982 and 1985 and the Millon Clinical Multiaxial Inventory (MCMI)<sup>25,26</sup> in 1987 and 1992. The MMPI is a 566-item self-administered questionnaire that evaluates personality status and emotional adjustment. Subjects were asked to determine whether the items are descriptive of them by rating each item as either "true" or "false." Standard scoring procedures produced scores for 4 validity scales and 10 clinical or personality scales. Raw scores were converted into standardized or T-scores, which have a mean of 50 and a standard deviation of 10. The validity scales included the cannot say (?) scale (total number of items omitted or double marked), the L-scale (identifies intentional efforts to evade responding frankly or honestly), the F-scale (a validity scale designed to detect unusual responding), and the K-scale (designed to detect subtle attempts to deny or exaggerate psychopathology). The basic clinical scales included the following scales. Scale 1 (hypochondriasis) assessed characteristics related to a pattern of hypochondriasis or abnormal concern for bodily func-

tions. Scale 2 (depression) assessed a clinical symptom pattern of depression. Scale 3 (hysteria) assessed hysterical reactions to stress situations, especially characteristics associated with the conversion form of hysteria. Scale 4 (psychopathic deviate) assessed characteristics of antisocial or psychopathic personality disorders. Scale 5 (masculinity-femininity) assessed sexual inversion. Scale 6 (paranoia) assessed a clinical pattern of paranoia. Scale 7 (psychasthenia) assessed characteristics of obsessive-compulsive traits. Scale 8 (schizophrenia) assessed a pattern of bizarre or unusual thoughts or behavior and other characteristics associated with schizophrenia. Scale 9 (hypomania) assessed characteristics of hypomania, such as overactivity, emotional excitement, and flight of ideas. Scale 0 (social introversion) assessed social uneasiness or a tendency to withdraw from social contacts.

On the MMPI, we analyzed K-corrected T-scores for each of the basic MMPI scales<sup>24</sup> and defined abnormal on these scales as a T-score of 70 or greater. We also analyzed Keane's post-traumatic stress disorder (PTSD) subscale and defined a raw score of greater than 30 as abnormal.<sup>27</sup>

The MCMI is a 175-item self-administered questionnaire that assesses both basic personality characteristics and clinical disorders. As with the MMPI, items are rated as "true" or "false." Standard scoring resulted in scales in three categories: basic personality patterns, pathological personality disorders, and clinical symptom syndromes. The basic personality pattern scales assessed enduring and pervasive traits that characterized styles of behavior, thinking, feeling, and relating to others. These included scale 1 (schizoid [asocial]), scale 2 (avoidant), scale 3 (dependent [submissive]), scale 4 (histrionic [gregarious]), scale 5 (narcissistic), scale 6 (antisocial [aggressive]), scale 7 (compulsive [conforming]), and scale 8 (passive-aggressive [negativistic]). The pathological personality disorder scales assessed chronic or severe pathology in personality structure. These scales included scale S (schizotypal [schizoid]), scale C (borderline [cycloid]), and scale P (paranoid). The clinical symptom syndrome scales assessed pathological states usually triggered by external events. These included scale A (anxiety), scale H (somatoform), scale N (hypomanic), scale D (dysthymic), scale B (alcohol abuse), scale T (drug abuse), scale SS (psychotic thinking), scale CC (psychotic depression), and scale PP (psychotic delusions).

On the MCMI, we analyzed the base rate scores for the personality patterns, the pathological personality disorders, and the clinical symptom syndromes. We used the weight factor to adjust the scores for the scales in the latter two categories. The weight factor moderated the effects of excessive defensiveness and self-enhancement or emotional complaining and self-deprecation.<sup>25</sup> Because we were interested in examining the presence of personality and symptom syndromes, we used a base rate score of 75 or greater as our definition of abnormal on the MCMI scales.<sup>25</sup>

### Dioxin Assessment

In 1987, blood from willing participants was collected and assayed for dioxin.<sup>28</sup> Participation was voluntary, and consent forms were signed at the examination site. Veterans with no quantifiable dioxin result in 1987, those who refused in 1987, and subjects new to the study in 1992 were also asked to give blood for the assay at the 1992 examination. We estimated the

initial dioxin dose at the end of the tour of duty in Vietnam in Ranch Hand veterans having current dioxin levels above background (above 10 parts per trillion (ppt)) using a constant half-life of 8.7 years.<sup>29,30</sup> We assigned each veteran to one of four exposure categories, named "comparison," "background," "low," and "high," according to his group (comparison or Ranch Hand), current dioxin level, and initial dioxin level, defined in Table I. The cutoff point of 10 ppt or less was selected for the comparison and background categories because this value represents the 98.5 percentile of the comparison population and, thus, is the value we regard as a threshold for background dioxin exposures.<sup>31</sup> The cutoff point separating the low and high dioxin categories (94 ppt) was the median initial dioxin level among all Ranch Hand veterans having current dioxin levels greater than 10 ppt. Thus, this value was selected as it results in approximately balanced sample sizes in the low and high categories. Table I shows the number of subjects in each dioxin exposure category by examination year.

### Sample Size

Table II shows study sizes for the comparison and Ranch Hand veterans by examination year for the MMPI and MCMI analyses. We excluded from all statistical analyses veterans with no dioxin measurement, those with a nonquantifiable dioxin result, and comparison veterans with a dioxin result more than 10 ppt. When we computed frequency distributions of missing responses, we found a highly unusual number of veterans were missing answers to exactly 23 questions on the 1982 administration of the MMPI. When we examined the raw values, we found that 30 veterans (15 Ranch Hands and 15 comparisons) had strings of 23 consecutive missing answers with the strings appearing at different locations and with no apparent pattern. Because we were unable to explain these missing responses, we excluded these 30 veterans from the analyses. We excluded one Ranch Hand veteran who was not administered the MMPI inventory in 1982 due to illness. In addition, at the 1985 examination, two comparison veterans left 30 or more MMPI questions unanswered, and we excluded their results as being uninterpretable. We also excluded from the MCMI analyses any veteran with a sum of raw scores for scales 1 through 8 less than 94 or more than 165 (indicating an unusual need to conceal personal difficulties or to exaggerate emotional disturbances) or with a validity index greater than 1 (suggesting careless, random, or confused responding).<sup>26</sup>

Not indicated in Table II, retrieval of raw individual item MMPI

responses was not possible for 463 veterans at the 1982 assessment. Hence, we excluded these 463 veterans from the analysis of PTSD but included them in the other MMPI analyses because their summary scale scores were available.

### Data Analysis

We used logistic regression to compute the point estimate of the odds ratio and associated 95% confidence interval of having an elevated (abnormal) MMPI or MCMI scale score using SAS PROC LOGISTIC (SAS Institute Inc., Cary, North Carolina). Ranch Hand veterans with background, low, and high dioxin exposures were each contrasted with the veterans in the comparison dioxin group. We adjusted for age (continuous, in years), race (black, non-black), rank (officer, enlisted), marital status (married, not married), and combat exposure level using a combat index developed for this study. Combat exposure was controlled in the analyses due to its known association with psychological outcomes among Vietnam veterans. The combat index was computed as a weighted sum of indicators of positive responses to 15 questions with positive ("yes") responses indicated by 1 and negative ("no") responses indicated by 0. The questions and associated weights for the combat index are shown in Table III. Each veteran was assigned to one of four strata depending on whether his sum fell into the ranges 0 to 2, 3 to 5, 6 to 8, or 9 and over, which were the approximate quartiles of the distribution. Combat index stratum was indicated in the logistic regression model by three dummy covariates. We used main effects models throughout without any stepwise reduction. (Odds ratios and confidence intervals are not shown and are available on request.)

When the number of veterans with an elevated MMPI or MCMI scale score was small, there were sometimes no veterans with scores in the abnormal range having a particular value of a discrete covariate, meaning that the covariate could not be used to adjust the logistic regression. Whenever this happened, we removed the covariate for all logistic models involving the likelihood of that abnormality.

In logistic regression, the odds ratio is an estimate of the magnitude of the association between an exposure and a dichotomous outcome after simultaneous adjustment for potential confounding factors.<sup>32</sup> An odds ratio of 1.0 (the null value) indicates no association between the exposure and the outcome. A value greater than 1.0 indicates a positive association or an increase in the odds of an outcome occurring given a particular level of exposure. A value less than 1.0 indicates an inverse

TABLE I  
EXPOSURE CATEGORY DEFINITION AND ASSOCIATED SAMPLE SIZES AMONG U.S. AIR FORCE VETERANS WHO SERVED IN SOUTHEAST ASIA FROM 1962 TO 1971

Dioxin Category	Definition <sup>a</sup>	Examination Year			
		1982	1985	1987	1992
Comparison	D ≤ 10	1,037	1,152	1,202	1,195
Ranch Hand					
Background	D ≤ 10	382	401	403	400
Low	10 < D and I ≤ 94	268	268	275	260
High	10 < D and 94 < I	271	279	275	267
Total Ranch Hand		921	948	953	927
Total		1,958	2,100	2,155	2,122

<sup>a</sup> D, dioxin measured in 1987 or 1992; I, dioxin extrapolated to the time of departure from Southeast Asia.

TABLE II  
SAMPLE SIZES BY EXAMINATION YEAR AMONG U.S. AIR FORCE VETERANS WHO SERVED IN SOUTHEAST ASIA FROM 1962 TO 1971

Veterans	MMPI		MCMI	
	1982	1985	1987	1992
<b>Comparison</b>				
Participated in physical examination	1,223	1,292	1,298	1,280
No dioxin measurement	-111	-70	-26	-23
Nonquantifiable dioxin result	-36	-41	-43	-34
Dioxin > 10 ppt <sup>a</sup>	-24	-25	-25	-24
Unexplained missing MMPI data <sup>b</sup>	-15			
Refused psychological testing		-2	-1	-2
MMPI not administered				
MMPI uninterpretable <sup>c</sup>		-2		
MCMC exclusions:				
Sum of scales 1-8 invalid			-1	-2
Validity index >1				
Net	1,037	1,152	1,202	1,195
<b>Ranch Hand</b>				
Participated in physical examination	1,046	1,017	996	953
No dioxin measurement	-93	-51	-24	-12
Nonquantifiable dioxin result	-15	-16	-15	-10
Unexplained missing MMPI data	-15			
Refused psychological testing	-1	-2	-3	-1
MMPI not administered	-1			
MMPI not interpretable				
MCMC exclusions:				
Sum of Scales 1-8 invalid				-3
Validity index >1			-1	
Net	921	948	953	927

<sup>a</sup> Parts per trillion.

<sup>b</sup> Subjects excluded because of unexplained strings of 23 consecutive unanswered questions on the MMPI.

<sup>c</sup> MMPI considered uninterpretable if 30 or more MMPI questions were unanswered.

TABLE III  
QUESTIONS AND ASSOCIATED WEIGHTS FOR COMPUTING THE COMBAT INDEX

Question	Weight
Did you receive combat pay?	1
Did you crash land, bail out, or were you shot down?	1
Did you receive sniper or sapper fire in or around the base?	1
Did you move killed or wounded personnel?	2
Did you serve as a forward air controller?	1
Did you fly in the same aircraft when a fellow crew member was wounded or killed?	2
Did you fly in the same formation or the same sortie when a fellow crew member was wounded or killed?	1
Did you fly in an aircraft that received battle damage?	1
Did you receive incoming artillery or rocket fire at your home base or camp?	1
Did you encounter mines or booby traps?	1
Did you kill Viet Cong or North Vietnamese Army in strafing or bombing runs?	2
Were you wounded?	2
Was a close friend killed in action?	2
Did you engage Viet Cong or North Vietnamese Army in a firefight?	2
Were you captured by the enemy?	2

association or a decrease in the odds of an outcome. The 95% confidence interval around the odds ratio estimate is calculated using the  $\beta$ -coefficient for the exposure variable and its stan-

dard error. Confidence intervals that exclude 1.0 indicate statistical significance at the 0.05 probability level.

We also calculated the mean T-score for the basic MMPI scales and the mean base rate scores the MCMI scales to provide information on the overall clinical profiles among veterans in the four dioxin categories. We used data from the examination dates closest to the exposure (i.e., the 1982 examination for the MMPI data and the 1987 examination for the MCMI data).

## Results

Demographic characteristics of all veterans are presented in Table IV. Ranch Hand veterans in the high dioxin category were slightly younger on average than those in the low and background categories. Most of the Ranch Hand veterans in the high dioxin category were enlisted personnel and those in the background category were predominantly officers. At the 1987 assessment, the median dioxin level was 14.9 ppt (range, 10.0-25.6 ppt) for Ranch Hand veterans in the low category and 45.7 ppt (range, 18.0-617.8) for Ranch Hand veterans in the high category. The intervals overlap because these categories were defined by initial rather than measured dioxin level.

## MMPI Findings

We found few associations between dioxin level and clinical elevations on the MMPI scales, and the direction and patterns of the significant associations were inconsistent. In the 1982 assessment, Ranch Hand veterans in the high dioxin category

TABLE IV

DISTRIBUTION OF DEMOGRAPHIC CHARACTERISTICS BY DIOXIN EXPOSURE CATEGORY AMONG U.S. AIR FORCE VETERANS WHO SERVED IN SOUTHEAST ASIA FROM 1962 TO 1971

Dioxin Category	Dioxin <sup>a</sup> (ppt) Median (range)	Initial Dioxin (ppt) Median (range)	Age <sup>c</sup> (Years), Mean (SD)	Officer (%)	Black (%)	Combat Index Median (range)
Comparison	4.0 (0-10)		53.2 (7.5)	39.3	5.2	5 (0-17)
Ranch Hand Background	5.7 (0-10)		54.2 (7.0)	61.5	5.0	6 (0-17)
Low	14.9 (10-26)	52.3 (27-94)	54.8 (7.7)	40.0	8.5	6 (0-19)
High	45.7 (18-618)	194.7 (94-3,290)	50.8 (7.3)	3.0	4.9	4 (0-18)

<sup>a</sup> Based on the 2,122 veterans who participated in the 1992 physical examination.<sup>b</sup> Parts per trillion.<sup>c</sup> Age at the 1992 physical examination.

were 50% more likely than comparison veterans to have elevations on scales 2 (depression) and 3 (hysteria); however, these odds ratios were of borderline significance as the lower limit of the 95% confidence interval was 1.0. Ranch Hand veterans in the low dioxin category were 60% more likely than comparison veterans to have an elevated scale 7 (psychasthenia). We also found some significant associations in our comparison of Ranch Hand veterans with background dioxin levels and the comparison veterans. These Ranch Hand veterans were approximately three times more likely than comparison veterans to have an elevated F (validity) scale and approximately two times more likely than comparison veterans to have an elevated scale 8 (schizophrenia).

No significant positive associations between dioxin level and clinical elevations on the MMPI scales were found in the 1985 assessment. Rather, Ranch Hand veterans in the high category were 60% less likely than comparison veterans to have an elevated scale 5 (masculinity-femininity) and 40% less likely than comparison veterans to have an elevated scale 9 (hypomania). There were no significant associations between dioxin exposure category and elevations on Keane's PTSD scale at either assessment period.

### MCMI Findings

Contrasts between Ranch Hand exposure categories and the comparison category revealed that only veterans in the background category were significantly more likely to have elevated MCMI scale scores with all of these occurring on the 1992 administration of the MCMI. These elevations were primarily in the basic personality patterns. Ranch Hand veterans in the background category were approximately two times more likely than comparison veterans to have elevated base rate scores on scales 1 (schizoid), 2 (avoidant), 8 (passive-aggressive), and P (paranoid). These veterans were also 50% more likely than comparison veterans to have elevated base rate scores on scale 6 (antisocial) and 20% more likely to have elevations on scale 5 (narcissistic). In addition, Ranch Hand veterans in the background category were two times more likely than comparison veterans to report symptoms suggestive of a psychotic delusional disorder (scale PP, psychotic delusions).

Ranch Hand veterans in the high dioxin category scored similarly to comparison veterans on the MCMI. The one exception was on the 1987 assessment; Ranch Hand veterans in the high

category were less likely than comparison veterans to report symptoms suggestive of a somatoform disorder (scale H, somatoform).

Similarly, there were few differences between Ranch Hand veterans in the low dioxin categories and comparison veterans on the MCMI. There were a few negative associations noted; however, for most of these associations, the upper confidence limit was equal to 1.0. In the 1987 administration of the MCMI, Ranch Hand veterans within the low category were less likely than comparison veterans to have elevations on scale 3 (dependent), scale H (somatoform), and scale T (drug abuse). In 1992, Ranch Hand veterans in the low category were less likely than comparison veterans to have elevations on scale 1 (schizoid) and scale T (drug abuse).

### Clinical Profiles

The mean scale scores for the MMPI and MCMI are graphically represented in Figures 1 and 2, respectively. These graphs illustrate that, on the average, the response patterns on these two psychological inventories were similar among all four groups of veterans.

### Discussion

The development of a serum assay for dioxin has allowed the measurement of an objective marker of dioxin exposure.<sup>30</sup> Studies suggest that most veterans who served in Vietnam were not heavily exposed to dioxin.<sup>33</sup> The exceptions to this are veterans who were involved in handling herbicides, such as those assigned to the Ranch Hand Operation. Even among Ranch Hand veterans, there is a range of dioxin exposure with serum dioxin levels measured in 1987 ranging from 0 to 618 ppt. Due to the long half-life of dioxin, approximately 9 years, this study shows that high levels can be measured 20 or more years after heavy exposure.

In this study, we measured dioxin in serum collected in 1987 and 1992, which allowed us to estimate the level of exposure at the time of the Vietnam War among those with dioxin levels above background and assigned each Ranch Hand veteran into one of three exposure categories. In contrasts of Ranch Hand veterans with comparison veterans with no known occupational exposure, we found few consistent differences in psychological functioning.

The U.S. Air Force Health Study of Ranch Hand veterans provides a unique opportunity to assess the relation between



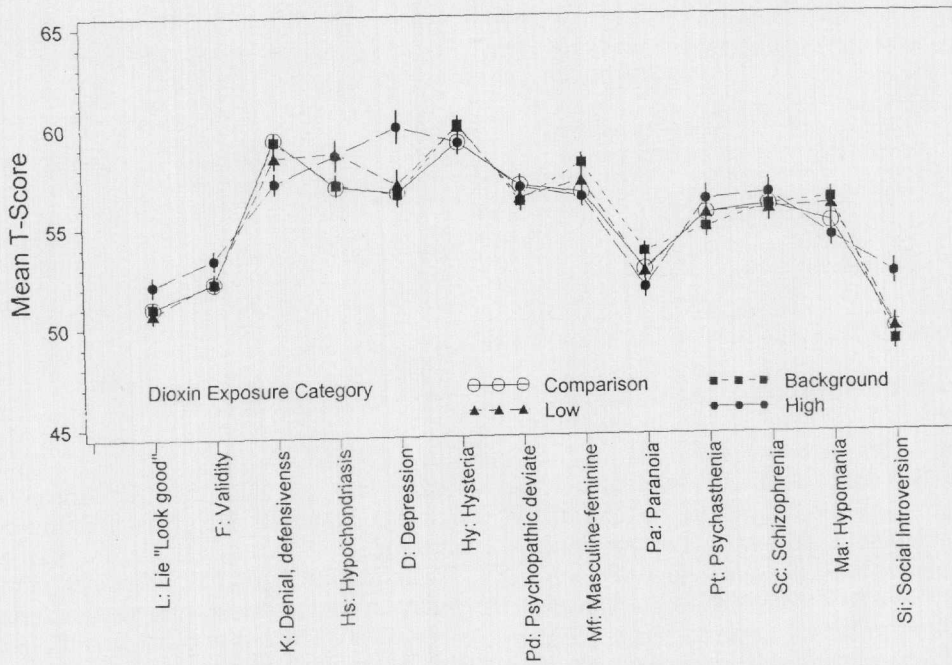


Fig. 1. Mean T-scores for the MMPI basic scales by dioxin exposure category, 1982 examination. Error bars extend to mean  $\pm$  1 SE.

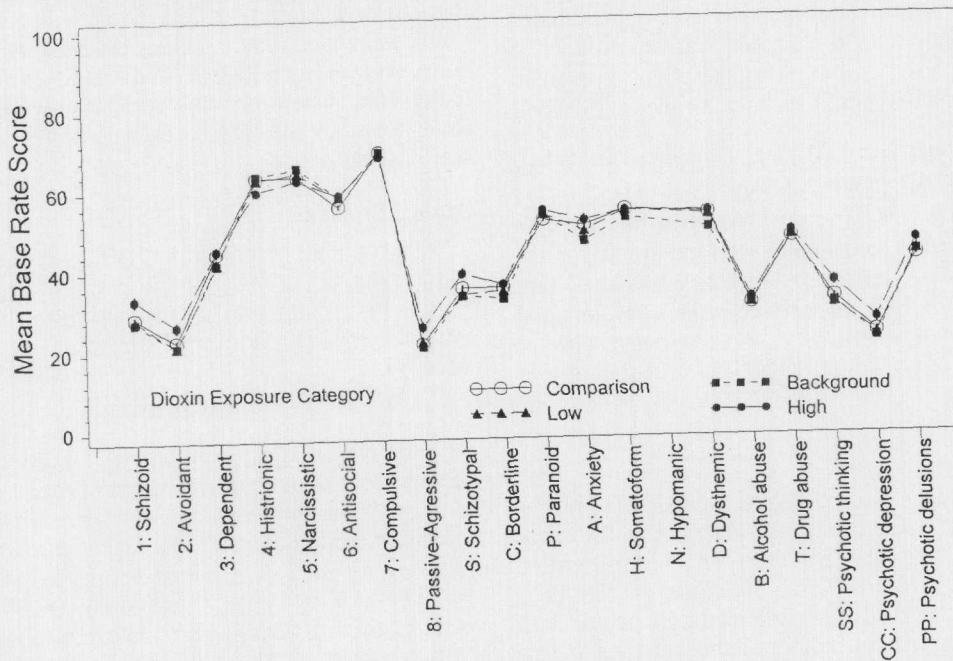


Fig. 2. Mean base rate scores for the MCMI scales by dioxin exposure category, 1987 examination. Error bars extend to mean  $\pm$  1 SE. The error bars are partially hidden by the symbols because the SE was less than 1.6 units for all scales.

dioxin exposure and psychological functioning. This is the only study that has followed a large number of Vietnam veterans with a high likelihood of exposure to Agent Orange and included objective, standardized tests to assess dioxin exposure and psychological functioning. The results of this study suggest that there are few consistent psychological abnormalities associated with dioxin exposure among these veterans. Ranch Hand veterans in the low or high dioxin categories showed indications of anxiety, somatization, and depression and a denial of psycho-

logical factors as measured by the MMPI. However, those in the background category also showed indications of distress both on the MMPI and the MCMI. This consisted primarily as emotional numbing and lability, a guarded, suspicious, and withdrawn style of relating to others, and unusual thoughts or behaviors most likely related to their high level of distress.

We found no association between dioxin exposure category and PTSD symptoms as measured on the MMPI. PTSD is a well-documented health outcome of the Vietnam War and is

associated with the extent of combat exposure.<sup>1</sup> Combat exposure, measured by our combat index, was not related to dioxin exposure category in this study.

Our ability to detect associations was limited by the fixed size of the Ranch Hand cohort. Because all Ranch Hand veterans have been identified and invited to participate in the study, their number could not be increased. The rarity of some of the abnormalities we studied led to imprecise measures of association, as indicated by wide confidence intervals, and small numbers prevented us from strong inferences among the most heavily exposed veterans. Confounding was another concern. Although we adjusted for all known confounders, there is the possibility that others existed that we did not take into account.

This study was limited by uncertainties regarding dioxin exposure. The serum dioxin measurements were accurate<sup>34</sup> and correlated with reported skin exposure to herbicide in Vietnam<sup>35</sup> but were made up to 30 years after exposure. Our initial dose calculation was based on a first order decay law with an assumed constant half-life. Changes in body fat may have altered the half-life in some individuals, causing us to misclassify some Ranch Hand veterans. Furthermore, we regard the background category as a mixture of exposed and unexposed veterans whose true status could not be determined with available data. The time since exposure varies between 15 and 26 years, which is approximately two or three dioxin half-lives. The elimination of dioxin in the intervening years and lack of alternative evidence of exposure left the exposure status of Ranch Hand veterans having background levels (below 10 ppt) unresolvable.

It is unclear from these findings to what extent these problems relate to the veterans' continued concern regarding the health impact of herbicide exposure. Another study has found that Vietnam veterans who report high Agent Orange exposure were more concerned about the future health effects of dioxin than they were worried about the actual effects of dioxin to date.<sup>23</sup> Advances in analytical chemistry have enabled us to measure dioxin to more directly assess Vietnam veterans' exposure to Agent Orange and other contaminated herbicides. However, this information was provided to veterans many years after exposure. The importance of having techniques to quickly assess exposure to potentially toxic agents is further highlighted by the experience of Gulf War veterans. In the absence of this information, veterans are left with fears regarding not only their own health, but also the health of their family members. Further development of techniques that will permit a rapid assessment of exposure to chemical agents may help reduce veterans' fears in future deployments.

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