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Dioxins and Dioxin-Like Chemicals in Blood and Semen of American Vietnam Veterans From the State of Michigan

Arnold Schecter, MD, MPH, Harry McGee, MPH, John S. Stanley, PhD, Kathy Boggess, PhD, and Paul Brandt-Rauf, MD, ScD, DrPH

This exposure assessment pilot study tested the hypothesis that elevated blood levels of the dioxin congener 2,3,7,8-TCDD ("TCDD"), due to Agent Orange exposure, in American Vietnam veterans could be demonstrated two to three decades after Vietnam service. A second objective was to determine if dioxins, including TCDD, are present in the semen of adult males. In the early 1990s, blood samples from 50 Vietnam veterans and three pooled semen samples from 17 of them were analyzed by high-resolution gas chromatography–mass spectroscopy for dioxins, dibenzofurans, and the dioxin-like PCBs. Fifty volunteers from the Michigan Vietnam veteran bonus list, which documented Vietnam service, were invited to participate based on their self-reported exposure to Agent Orange in Vietnam. Screening of military and medical records was performed by an epidemiologist and a physician to assure that Agent Orange exposure was possible based on job description, location of service in Vietnam, and military Agent Orange spray records. Elevated 2,3,7,8-TCDD levels, over 20 ppt on a lipid basis, could still be detected in six of the 50 veterans in this nonrandomly selected group. The dioxin and dibenzofuran congeners commonly found in the U.S. population, including TCDD, were also detected in the three pooled semen samples. Quantification and comparison on a lipid basis were not possible due to low lipid concentrations where levels were below the detection limit. Therefore, semen samples were measured and reported on a wet-weight basis. Elevated blood TCDD levels, probably related to Agent Orange exposure, can be detected between two and three decades after potential exposure in some American veterans. Original levels were estimated to be 35–1,500-fold greater than that of the general population (4 ppt, lipid) at the time of exposure. In addition, the detection of dioxins in semen suggests a possible mechanism for male-mediated adverse reproductive outcomes following Agent Orange or other dioxin exposure. © *1996 Wiley-Liss, Inc.*

KEY WORDS: dioxins, dibenzofurans, PCBs, Vietnam veterans, blood, semen, dioxin toxic equivalents

INTRODUCTION

In the U.S.–Vietnam War, between 1962 and 1971, fixed wing aircraft spraying of Agent Orange was conducted in order to protect U.S. and allied forces by defoliating jungle cover used by enemy troops, and to destroy the crops which fed the enemy. The use of Agent Orange resulted in fears about chemical exposure and adverse health effects, for both Vietnam veterans and Vietnamese, which persist today, decades after the war officially ended in 1975.

Dioxins are synthetic, lipophilic, toxic chemicals of re-

Department of Preventive Medicine, Clinical Campus, State University of New York, Health Science Center—Syracuse, Binghamton (A.S.).
Chronic Disease Section, Michigan Department of Public Health, Lansing (H.M.).
Midwest Research Institute, Kansas City, MO (J.S.S., K.B.).
Division of Environmental Sciences, School of Public Health, Columbia University, New York, NY (P.B.-R.).
Address reprint requests to Arnold Schecter, MD, MPH, Department of Preventive Medicine, Clinical Campus, State University of New York, Health Science Center—Syracuse, 88 Aldrich Avenue, Binghamton, NY 13903.

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cent origin [Czuczwa et al., 1984, 1986; Schecter et al., 1988, 1991; Tong et al., 1990]. The most toxic of these, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), or simply dioxin, was an unwanted contaminant present in Agent Orange.

Agent Orange, named for the orange identification stripe on the drums containing the herbicide, was a half and half mixture of two phenoxyherbicides, the n-butyl esters of 2,4-dichloro-phenoxyacetic acid (2,4-D) and 2,4,5-trichloro-phenoxyacetic acid (2,4,5-T). Agent Orange was contaminated with an average of 2–3 parts per million (ppm) of TCDD [NAS, 1974], with some lots containing 30–90 ppm. Between 12 and 20 million gallons of herbicides containing TCDD were applied to discrete areas in the south and central parts of Vietnam—"South Vietnam"—below the 17th parallel, from 1962 through 1970; 88% was applied by fixed wing aircraft, and the remaining 12% was sprayed from backpacks, helicopters, or naval vessels [Westing, 1984; Young, 1988; Institute of Medicine, 1994]. Agent Orange was by far the herbicide most commonly used for defoliation by the U.S. Military in Vietnam.

Although the question of Agent Orange exposure and health consequences has long been of concern, valid health studies are not possible without adequate characterization of exposure. In a Massachusetts pilot study of Agent Orange, we previously found elevated TCDD in adipose tissue and blood of Vietnam veterans up to 18 years after exposure [Schecter et al., 1989, 1987, 1990]. This paper describes a similar pilot study conducted for the State of Michigan to determine (1) whether elevated levels of dioxin-like chemicals including TCDD could be found in veterans' blood long (19–29 years) after possible exposure in Vietnam, and (2) whether any dioxins are present in the semen of these adult males, something which has not been previously detected in human semen.

Elevation of blood 2,3,7,8-TCDD is characteristic of Agent Orange exposure. However, because total dioxin toxicity is not determined by TCDD alone, we measured all of the toxic polychlorinated dibenzo-p-dioxins (PCDDs) and closely related polychlorinated dibenzofurans (PCDFs), those with chlorine in the 2, 3, 7, and 8 positions on the benzene rings. These chemicals are presently found in characteristic patterns (for any given geographical area) in the blood of general population adults. These patterns show "normal" background dioxin exposure for inhabitants of industrialized countries, unrelated to Agent Orange exposure.

Even this does not present an accurate picture of total dioxin toxicity since other synthetic organochlorines, including many of the polychlorinated biphenyls (PCBs), also have dioxin-like toxicity [Safe, 1990; Alhborg et al., 1994]. Although PCBs are believed to be, as a class, somewhat less toxic than the dioxins, they are currently present in humans living in industrial countries at considerably higher levels than the dioxins, and therefore we included measurement of the dioxin-like coplanar, mono-ortho and di-ortho PCBs.

This is the first Vietnam veteran study to measure all dioxin-like compounds, to calculate total dioxin toxicity, and to use new analytic techniques to measure these various dioxin-like compounds in the blood of Americans. In addition, this is the first study to measure dioxins in semen.

The concept of "2,3,7,8-TCDD equivalents" or simply "dioxin toxic equivalents" (TEQ) is commonly used to compare the toxicity of other less toxic dioxin and dioxin-like congeners to 2,3,7,8-TCDD. To calculate total dioxin toxic equivalents, the amount of each congener is multiplied by its "dioxin toxic equivalency factor" (TEF) and the resulting sum of all congeners equals the total dioxin toxic equivalents. TCDD is defined as having a TEF of 1.0, while other toxic dioxins and dibenzofurans, those with chlorines in the 2, 3, 7, and 8 position on the benzene rings, are weighted from 0.5 to 0.001.

The concept of TEF was first applied to an incident which occurred at a New York State office building in Binghamton, contaminated with PCBs, dioxins, and dibenzofurans, and the concept has since been experimentally validated in toxicological studies using various endpoints of dioxin toxicity [Eadon et al., 1994]. The current "International" 2,3,7,8-TCDD dioxin toxic equivalency values (I-TEQ) are generally accepted for dioxins and dibenzofurans [NATO, 1988a,b; USEPA, 1989].

Dioxin-like PCBs are assigned a similar weighting, although presently there is less certainty as to the toxicologically correct values for the more abundant PCB congeners [Safe, 1990; Ahlborg et al., 1994]. Recent studies indicate that the original proposed values for the dioxin-like toxicity of PCBs were conservative and may overestimate the risks by up to 1,000-fold [DeVito et al., 1993]. It should be noted that the toxicity of some PCBs is not dioxin-like and therefore is not considered in the TEF scheme [Schantz and Seegal, 1994].

Because the hypothesis has been proposed that male-mediated adverse reproductive outcomes following Agent Orange exposure might be related to the presence of dioxins in semen, a secondary goal of this study was to attempt to determine whether dioxins were actually present in semen and, if so, at what levels [Hatch, 1984; Hatch and Stein, 1986]. Individual veteran semen samples were initially collected for analysis. However, insufficient sample volume, low levels of dioxins, and low lipid content led to the decision to randomly pool the 17 individual specimens into three composite samples for analysis.

MATERIALS AND METHODS

Participant Selection

From March 1991 through July 1992, 50 veterans were selected from the Michigan Vietnam veteran bonus list,

which documented their Vietnam military service. These men—no women qualified—were chosen based on self-reports of Agent Orange exposure and/or history of cancer or having fathered children with birth defects. The number studied was limited by funding. Military records were reviewed and veterans were interviewed to find those with the most convincing history of possible Agent Orange exposure and no history of other likely special exposure to TCDD outside of Vietnam. Potential for exposure included spraying of Agent Orange, having been sprayed with what was thought to be Agent Orange, or combat service in sprayed areas, with defoliation as evidence that the spray was an herbicide [Westing, 1984; Young, 1988]. Institutional Review Board (IRB)–approved informed consent documents were read and signed by all participants. A subgroup of 17 of these veterans volunteered to contribute semen, which was analyzed in three randomly pooled samples in order to provide sufficient volume for dioxin analysis.

Chemical

One unit (450 ml) of whole blood was collected from nonfasting participants between March 1991 and July 1992 at hospital blood banks, in standard plastic blood bank containers containing an anticoagulant. Individual semen samples, up to 100 ml, were collected in chemically cleaned glass containers with Teflon liners. All specimens were placed in chemically clean containers, frozen after collection at −20°C, and stored at that temperature until processed for analysis. Individual analyses were performed on blood samples.

Composite semen samples were needed to provide sufficient volume to identify and quantitate congeners. Composite 1 was semen from seven veterans, with a total weight of 325.41 g; Composite 2 was from six veterans, with a total weight of 419.37 g; and Composite 3 was from four veterans, with a total weight of 359.76 g. The mean dioxin levels of the three pooled samples is reported in this paper.

Analytic methodology consisted of high-resolution gas chromatography and high resolution mass spectroscopy (HRGC/HRMS), previously described in detail [USEPA, 1990; Dewailly et al., 1991; WHO, 1991; Boggess et al., 1993; Stanley et al., 1986; CDC, 1988; Stanley et al., 1990]. Analyses were performed at Midwest Research Institute (MRI). This laboratory has been certified by the World Health Organization for measurement of dioxins, dibenzofurans, and PCBs in human milk or blood [WHO, 1991].

Semen samples were prepared using procedures identical to those used for the blood, as described in EPA Method 8290 [USEPA, 1990; Boggess and Stanley, 1993].

RESULTS

In this study of 50 male Michigan Vietnam veterans, six (12%) were found to have elevated TCDD levels (≥10 ppt). All six had levels above 20 parts per trillion (ppt) on a lipid-adjusted basis, as shown in Figure 1. In a study of the general U.S. population surveying human tissue dioxin levels for the United States Environmental Protection Agency, 2,3,7,8-TCDD adipose tissue levels in pooled samples ranged from not detected (ND), with a detection limit of 1 ppt, to 10 ppt [Stanley et al., 1986]. Four of our 24 Army (17%) and two of our 14 Air Force personnel (14%) had blood TCDD levels above 10 ppt. Of the seven former Marines, four Navy veterans, and one Coast Guard veteran, none had TCDD levels above 10 ppt. A blood TCDD level above 10 ppt is generally considered to be elevated in comparison with the general U.S. population blood or adipose tissue dioxin TCDD level (mean 3–4 ppt) [Kahn et al., 1988; CDC, 1988; Schecter et al., 1989; Stanley et al., 1990; Schecter, 1991, 1992, 1994].

The first 23 veterans were selected because of a self-reported history of having handled Agent Orange; of these, five (22%) had elevated TCDD. No further volunteers were found with a history of actually handling Agent Orange. The remaining 27 included in the study were selected from veterans with possible Agent Orange exposure based on service history, and with either a history of cancer or of fathering a child with an adverse reproductive outcome, documented by medical records. Of these 27, only one (3.7%) had an elevated TCDD level.

Table I presents the mean and range of the 34 dioxin, dibenzofuran, and dioxin-like PCB congeners measured in whole blood for the 50 veterans; the dioxin toxic equivalency factors (TEFs); and their dioxin toxic equivalents (TEQs). Measured levels of TCDD, the dioxin characteristic of Agent Orange, varied from 0.88 to 131 ppt, with a mean level of 8.98 for all 50 veterans. Measured TCDD levels for the 44 veterans with levels below 10 ppt ranged from 0.88 to 8.3, with a mean level of 3.8, approximately the mean (3.5 ppt) TCDD level in blood or adipose tissue for the U.S. general population at the present time (median 3.05; range 0.95–7.7 ppt) [CDC, 1988; Stanley et al., 1990; Schecter, 1994, 1991, 1992].

Although previous Vietnam veteran studies focused initially on TCDD levels and later considered all dioxins and dibenzofurans, they did not consider the dioxin-like coplanar, mono-ortho and di-ortho PCBs. These chemicals have only lately been measured in human tissue and are shown on the bottom half of Table I [Schecter et al., 1987, 1989a,b, 1990; Weerasinghe et al., 1986; Patterson et al., 1986; Kahn et al., 1988].

Total measured dioxins in the blood of these veterans averages 1,025 ppt (range 319–3,836); the dibenzofurans average is lower, 67 ppt (range 26–193); coplanar PCBs average 229 ppt (range 40–867); mono-ortho PCBs average 50,000 ppt (range 5,509–299,316); and di-ortho PCBs average over 100,000 ppt (range 21,364–403,578), on a lipid basis in whole blood.

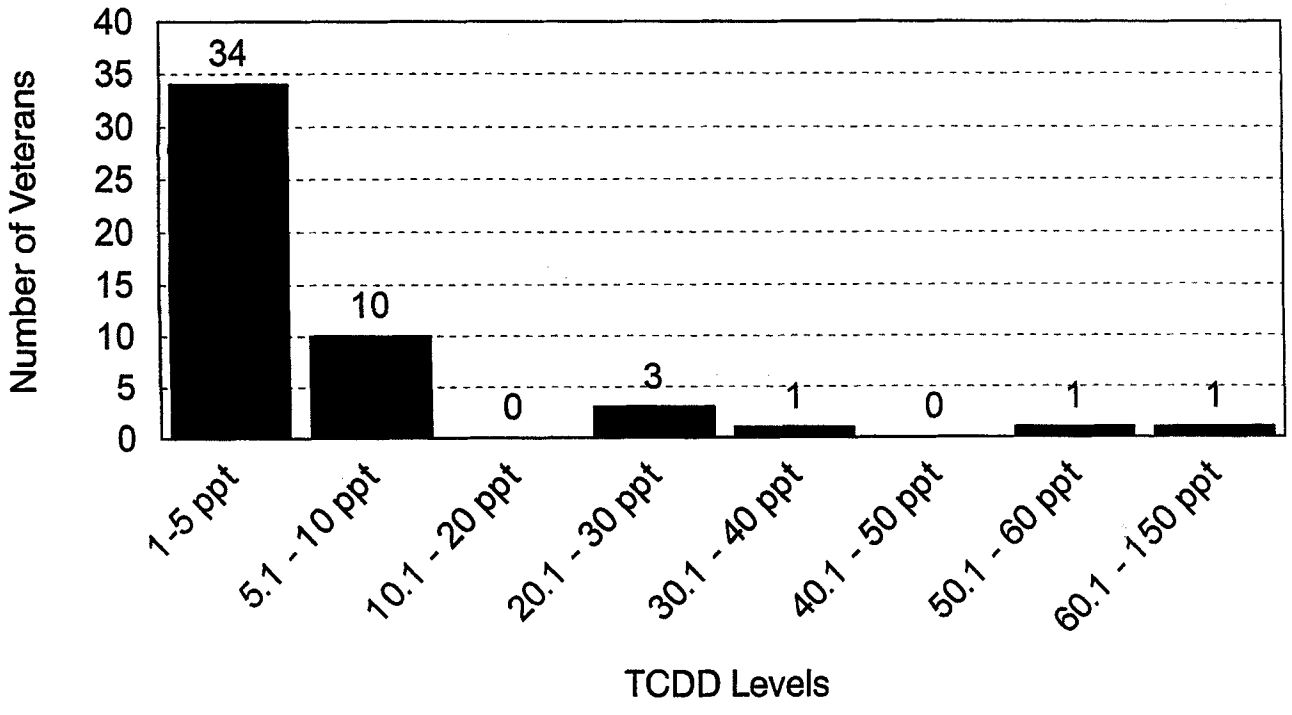

FIGURE 1. TCDD levels in whole blood of 50 Michigan Vietnam veterans 19–29 years after Vietnam service (ppt, lipid).

These values are measured levels, and reflect general environmental contamination and intake of dioxins, primarily from food, excluding the elevated TCDD levels. But they do not reflect the chemicals' dioxin toxicity, which is best characterized by converting to "dioxin toxic equivalents" (TEQs). The fifth column in Table I lists dioxin toxic equivalency factors (TEFs), and columns six, seven, and eight are the mean, minimum, and maximum dioxin toxic equivalents, respectively, for each chemical using the now commonly accepted "International" or Environmental Protection Agency (EPA) dioxin toxic equivalent factors for dioxins and dibenzofurans [NATO, 1988a,b; USEPA, 1989]. The mean TEQ value for the dioxins is 25 ppt (range from 5.97 to 178) and for the dibenzofurans 7 ppt (range from 1.67 to 23.03) TEQ (ppt, lipid). Total dioxin toxicity (total PCDD/Fs) averages 32 ppt and ranges from 7.6 to 201 TEQ (ppt, lipid) for all 50 veterans.

For the 44 veterans without TCDD elevation, TCDD averages 3.8 ppt (range 0.88–8.3) and total dioxin toxicity averages 26.6 ppt [range 7.6–78.3 TEQ (ppt, lipid)]. For all 50 veterans, TCDD contributes an average 8.98 ppt and ranges from 0.88 to 131.0 ppt.

In Table I, the PCBs are converted to dioxin toxic equivalents using the new World Health Organization (WHO)-proposed toxic equivalency factors, which are available for only eight congeners [Ahlborg et al., 1994]. At this time there are no accurate estimates for the dioxin-like toxicity of other detectable PCB congeners. Formerly, these other PCBs had relatively high estimated TEF values, which are now believed to overrate actual toxicity. The coplanar PCBs' mean dioxin toxicity contribution is 10 ppt (ranging from 2.3 to 44.4); the mono-ortho PCBs average 11.9 ppt (ranging from 0.4 to 28.3); and the di-ortho PCBs average 0.51 ppt (ranging from 0.12 to 2.82) on a lipid basis. Using these estimates of dioxin-like toxicity, the PCBs combined contribute an average of 22.5 ppt, with a range of 2.78–75.5 ppt. The mean grand total TEQ value for dioxin, dibenzofuran, and PCB is 54.3 ppt (range of 10.4–276.5).

Since TCDD is eliminated from the body slowly over time, the measured levels of TCDD in this study can be used to extrapolate back in time and estimate TCDD levels in the blood at the time of exposure. The span of time for these veterans, from the first possible exposure to having their blood drawn for this study, was an average of 26 years (ranging from 19 to 29 years). The six veterans with the highest TCDD blood levels were exposed approximately 23–24 years before this study's blood collection in the early 1990s.

Table II presents the measured and also the estimated blood levels of TCDD at time of exposure for the six veterans with elevated levels, calculated using both 5 and 10 year half-lives of elimination for TCDD, which approximate the best estimates available at this time [Poiger and Schlatter, 1986; Pirkle et al., 1989; Wolfe et al., 1994; Michalek et al., 1996]. Adjusting for dilution of TCDD in the lipid due to weight gain with aging [Werner, 1970;

TABLE I. Dioxin, Dibenzofuran, and PCB Levels, Dioxin Toxic Equivalency Factors (TEFs), and Dioxin Toxic Equivalents (TEQs) in Whole Blood of Michigan Vietnam Veterans 19–29 Years After Vietnam Service (ppt, Lipid, N = 50)

	Measured levels				Toxic equivalents		
Congeners	**Mean**	**Min**	**Max**	**TEFs**	**Mean**	**Min**	**Max**
Dioxins							
2,3,7,8-TCDD (<10 ppt) (N = 44)[c]	3.8	0.88	8.3	1	3.8	0.88	8.3
2,3,7,8-TCDD (N = 50)	8.98	0.88	131	1	8.98	0.88	131
1,2,3,7,8-PeCDD	9.3	3	35.5	0.5	4.63	1.48	17.75
1,2,3,4,7,8-HxCDD	9.8	2.3	22.2	0.1	0.68	0	2.22
1,2,3,6,7,8-HxCDD	72.1	27.3	168	0.1	7.21	2.73	16.8
1,2,3,7,8,9-HxCDD	11.9	3.1	35.9	0.1	1.19	1.31	3.59
1,2,3,4,6,7,8-HpCDD	119	32.1	333	0.01	1.19	0.32	3.33
1,2,3,4,6,7,8,9-OCDD	794	250	3110	0.001	0.79	0.25	3.11
Total dioxins	**1,025**	**319**	**3,836**		**24.7**	**5.97**	**178**
Dibenzofurans							
2,3,7,8-TCDF	2.3	0.6	7.3	0.1	0.23	0.06	0.73
1,2,3,7,8-PeCDF	1.2	0.6	4.9	0.05	0.06	0.03	0.25
2,3,4,7,8-PeCDF	8.8	1.9	29.2	0.5	4.38	0.93	14.6
1,2,3,4,7,8-HxCDF	10.6	2.5	43.1	0.1	1.06	0.25	4.31
1,2,3,4,6,8-HxCDF	6.9	2.3	14.6	0.1	0.61	0	1.46
2,3,4,6,7,8-HxCDF	2.8	1.4	6	0.1	0.28	0.14	0.6
1,2,3,7,8,9-HxCDF	2.8	1.5	5.1	0.1	0.28	0.15	0.51
1,2,3,4,6,7,8-HpCDF	19.6	9.7	49.1	0.01	0.2	0.1	0.49
1,2,3,4,7,8,9-HpCDF	3.1	1.5	4.8	0.01	0.03	0.01	0.05
1,2,3,4,6,7,8,9-OCDF	9.3	4.1	28.7	0.001	0.01	0	0.03
Total dibenzofurans	**67**	**26**	**193**		**7.14**	**1.67**	**23.03**
Total dioxins/dibenzofurans	**1,092**	**345**	**4,029**		**31.8**	**7.6**	**201**
Coplanar PCBs							
77 3,3,4,4-tetra PCB	79	10	336	0.0005[a]	0.04	0.01	0.17
126 3,3,4,4,5-penta PCB	104	22	432	0.1[a]	9.66	2.22	43.2
169 3,3,4,4,5,5-hexa PCB	46	8	99	0.01[a]	0.42	0.08	0.99
Total coplanar PCBs	**229**	**40**	**867**		**10.1**	**2.3**	**44.4**
Mono-ortho PCBs							
28 2,4,4-tri PCB	7,170	340	66,077	NA[b]	—	—	—
74, 2,4,4,5-tetra PCB	14,330	3,009	47,000	NA	—	—	—
105 2,3,3,4,4-penta PCB	6,928	1,500	37,039	0.0001[a]	2.58	0.15	3.7
118 2,3,4,4,5-penta PCB	16,213	330	125,000	0.0001[a]	3.67	0.03	12.5
156 2,3,3,4,4,5-hexa PCB	5,988	330	24,200	0.005[a]	5.66	0.17	12.1
Total mono-ortho PCBs	**50,629**	**5,509**	**299,316**		**11.9**	**0.4**	**28.3**
Di-ortho PCBs							
99 2,2,4,4,5-penta PCB	11,361	1,865	54,300	NA	—	—	—
128 2,2,3,3,4,4-penta PCB	2,104	215	12,000	NA	—	—	—
138 2,2,3,4,4,5-hexa PCB	26,297	5,540	102,000	NA	—	—	—
153 2,2,4,4,5,5-hexa PCB	40,055	7,140	123,000	NA	—	—	—
170 2,2,3,3,4,4,5-hexa PCB	6,620	814	23,400	0.0001[a]	0.13	0.08	2.34
180 2,2,3,3,4,4,5,5-hepta PCB	19,034	4,226	48,400	0.00001[a]	0.38	0.04	0.48
183 2,2,3,4,4,5,6-hepta PCB	2,534	484	10,061	NA	—	—	—
185 2,2,3,4,5,5,6-hepta PCB	1,284	205	7,360	NA	—	—	—
187 2,2,3,4,5,5,6-hepta PCB	7,378	875	23,057	NA	—	—	—
Total di-ortho PCB	**116,667**	**21,364**	**403,578**		**0.51**	**0.12**	**2.82**
Total PCBs	**167,525**	**26,913**	**703,761**		**22.54**	**2.78**	**75.48**
Grand total TCDD/Fs, PCBs	**168,617**	**27,258**	**707,789**		**54.34**	**10.38**	**276.48**

[a]Indicates WHO TEFs for these PCB calculations [Ahlborg et al., 1994].
[b]NA = TEF values have not been established.
[c]TEQs for 44 veterans without elevated TCDD levels are approximately equivalent to the general population.

TABLE II. Measured TCDD Blood Levels (1991–1992) and Estimated Level at Time of Exposure for Veterans With Elevated TCDD Levels (ppt, Lipid, 23–24 Years After Agent Orange Exposure)*

Patient number	Measured level	At exposure (5 yr half-life)	At exposure (10 yr half-life)
1107	131	6,006	1,138
1115	21.3	745	141
1111	20.4	800	151
1105	31	810	164
500	54.5	2,036	385
493	22.9	686	140

*Mean weight during service in Vietnam = 165 lbs (range 110–240 lbs); mean weight when samples obtained = 199 lbs (range 135–340 lbs).

TABLE III. Mean Dioxin and Dibenzofuran Levels of Three Pooled Semen Samples From 17 Adult Male Vietnam Veterans

	Semen	
	ppq wet weight	Mean TEQ
TCDD	3	0.003
PeCDD	4	0.002
Total HxCDD	38	0.004
HpCDD	89	0.001
OCDD	787	0.001
Total PCDDs	920	0.010
TCDF	1	0.0001
1,2,3,7,8-PeCDF	1	0.0002
2,3,4,7,8-PeCDF	3	0.002
Total HxCDF	13	0.001
Total HpCDF	6	0.00004
Total OCDF	177	0.00004
Total PCDFs	201	0.003
Total PCDD/PCDFs	1,121	0.013

Schecter et al., 1989], TCDD levels at time of exposure for these veterans probably ranged between 140 and 6,006 ppt on a lipid basis, or 35–1,500 times the average for the general population of approximately 4 ppt. Weights of the veterans were self-reported both at the time of military service and time of blood collection.

Total dioxin TEQ, not shown on Table II, would have been somewhat higher than these values and TCDD would have made a much larger contribution to total dioxin toxicity at initial exposure than it does at present. We calculated an average total dioxin toxic equivalent of about 78 ppt and a range from 14 to 398 ppt, with approximately 4 ppt from TCDD in the 44 veterans without elevated TCDD.

Table III presents the average levels of dioxins and dibenzofurans from three composite samples of semen from 17 of the veterans. It should be noted that the blood data are reported in parts per trillion, normalized on a lipid basis as is now customary, whereas the semen data, due to extremely low lipid levels, are reported in parts per quadrillion (ppq) on a wet-weight basis.

Measured values for semen dioxin analyses on a lipid basis were reported below the detection limit. Nondetected values on a wet-weight basis were reported using one-half the detection limit for calculating dioxin TEQs. Further, it was not technically possible to use equal amounts of semen in preparing semen specimens for analysis. Nevertheless, dioxin and dibenzofuran congeners are present and quantifiable in human semen, although it was not possible to compare blood and semen levels from the same subjects in this study.

DISCUSSION

In our previous Vietnam veteran studies, conducted closer to time of service in Vietnam [Schecter et al., 1987, 1989a/b, 1990], dioxin intake from Agent Orange was found in a minority of those veterans chosen who had a service history in Vietnam consistent with exposure, having been sprayed or worked in sprayed areas, which is similar to the present findings. In three previous major Vietnam veteran dioxin exposure studies, the Massachusetts [Schecter et al., 1987, 1989a/b, 1990], the Centers for Disease Control [CDC, 1988], and the New Jersey [Kahn et al., 1988], the majority of American Vietnam veterans, although selected from those thought likely to have been exposed, did not show evidence of Agent Orange exposure as determined by elevated TCDD fat or blood tissue levels, measured up to 18 years after Vietnam service.

Since the half-life of elimination of TCDD from the body is currently believed to be between 5 and 10 years [Wolfe et al., 1994; Michalek et al., 1996], only veterans with tissue levels of 2,3,7,8-TCDD between 40 and 50 ppt in Vietnam over 20 years ago would have blood TCDD levels above 10 ppt at the time of sampling in the early 1990s, assuming that they have had no other above background exposure since that time. Thus, even the highly sensitive and selective GC-MS measurement of dioxins in human tissue will no longer detect intake of TCDD from Agent Orange in Vietnam, except in veterans with exposure and initial tissue levels above that value.

Although we did find elevated TCDD above the U.S. mean level of 3–4 ppt, and here above 20 ppt, in six of 50 veterans, these were not from a representative sample of Vietnam veterans but instead were from veterans chosen for having a high likelihood of exposure to Agent Orange. These results may provide some reassurance for many Vietnam veterans, and their families, who probably were not exposed to Agent Orange due to the nature of their duties or

the location of their Vietnam assignments. The estimated 35–1,500-fold excess of TCDD above background at time of exposure in 12% of these veterans is cause for concern. It suggests the possibility of significant intake of dioxin from Agent Orange in at least some Vietnam veterans.

We have previously reported elevated 2,3,7,8-TCDD in the tissues of Vietnamese living in Vietnam, again documenting intake of dioxin from Agent Orange in another exposed population [Schecter et al., 1995]. Thus, dioxin intake does occur in some Agent Orange–exposed persons, whether from occupational exposure, as in the U.S. Vietnam veterans, or environmental exposure, as in the Vietnamese.

In addition, the existence of dioxins and dibenzofurans in semen of U.S. adult males, first documented in this study, is an area which requires further investigation. PCBs were previously found in semen and were found to decrease sperm motility in a dose-dependent fashion [Bush et al., 1986]; the presence of these additional xenobiotics, structurally and toxicologically similar to PCBs, may likewise cause harm to sperm. Future research will establish whether or not dioxins in semen at various levels are harmful. It is unlikely, however, that their presence would lead to beneficial consequences. Further research is indicated to determine if the elevated TCDD levels found in some veterans' blood is mirrored by a similar elevation in semen and, further, whether or not this leads to adverse reproductive health consequences [Rier et al., 1993]. Our semen data are not adequate to determine whether or not elevated TCDD from Agent Orange may be found in semen of some U.S. Vietnam veterans.

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