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TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) in Body Fat of Vietnam Veterans and Others

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Authors

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The past three years have seen a mounting concern over exposure to the defoliant 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), an ingredient of Herbicide Orange used by the United States Armed Forces in Vietnam from 1965 to 1971. At least some lots of 2,4,5-T contained a contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin, also called TCDD or simply "dioxin". This substance is highly toxic to animals (1,2) and has been claimed to produce chronic and delayed adverse effects among American veterans who served in Vietnam.

TCDD accumulates preferentially in the body fat of experimental animals (3) and man (4). It has been postulated to remain in adipose tissue for years and to threaten damage if released by reduction in the amount of that tissue (5).

Analytic methods to identify and measure TCDD have improved in recent years, enabling the Veterans Administration to investigate whether TCDD can be detected in the body fat of veterans who were presumably exposed to Herbicide Orange and in the fat of other veterans without known exposure to the herbicide. Three Air Force officers with more recent and better reported exposure to TCDD were tested as well.

Twenty veterans who believe that they were exposed to Herbicide Orange in Vietnam volunteered to have 10 to 30 grams of fat removed from their abdominal walls. Another ten veterans without known contact agreed to have a similar specimen of subcutaneous fat removed during an otherwise necessary abdominal operation. Three Air Force officers who volunteered for biopsy had been intimately involved with the destruction of Herbicide Orange, two years earlier, had had other frequent contacts with the herbicide, and had used TCDD in the laboratory.

The biopsies were conducted with care to avoid contamination by products containing TCDD. The specimens were collected in glass containers previously rinsed with acetone and refrigerated until use.

The methods of extraction and of gas chromatography - mass spectrography have been described by Gross (6). Ten specimens of the thirty-three were assayed as well in a second laboratory using slightly different techniques. The assays in both were conducted without knowledge of which specimens came from exposed and which from non-exposed men.

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Each of the twenty exposed volunteers provided information about his military service with details of his exposure to toxic substances in Vietnam or elsewhere. A medical history, physical examination, and routine clinical chemistry were obtained, although the values of the latter are not available in some instances. Service records were made available, as well. The clinical data were reviewed, seeking correlations between them and the assay results. The details of military service in Vietnam from the volunteer's report and his service record were examined in order to evaluate his likely exposure to Herbicide Orange using the dates, location, and nature of his service. From what is known of the times and places of Herbicide Orange usage a rough estimate of the likelihood of exposure was possible. This evaluation was made without knowledge of the assay results.

Results. The assay results are reported in Table I. Detailed tabulations of the results and comparisons with those from the second laboratory are given by Gross (6). It should be noted that where the assay is indicated as negative despite an apparently detectable amount of TCDD, the chemist was unable to identify the measured substance as TCDD. In such cases, contamination with small quantities of some other, unidentified substance is likely (6).

One of the three Air Force officers with known exposure to TCDD had no identified TCDD in his fat. The unidentified substance in his case and the TCDD measured in the other two officers was never more than 3 parts per trillion above the limit of detection.

Of the twenty veterans from Vietnam, seven (numbers 1,9,13,16,19,27 and 30) had no detectible TCDD with a limit of detection at 2 to 4 parts per trillion; another two (numbers 6 and 8) had detectible material that could not be validated as TCDD and one (number 14) could be considered equivocal because the measured value was so low as to be questionable. The ten remaining men had TCDD identified and measured in amounts from 3 parts per trillion with a limit of detection of 2 parts (number 11) to 96 or 100 parts per trillion with 10 parts limit of detection (number 26). Only one other (number 10) had a TCDD value greater than 7 parts per trillion above the limit of detection.

Of the 10 unexposed veterans, two (numbers 20 and 23) had TCDD identified in their fat; neither had more than 6 parts per trillion above the limit of detection. Two other veterans (numbers 17 and 23) had values low enough to be considered equivocal and in five instances (number 5,7,21,31, and 33) the detected material was not validated as TCDD. The remaining veteran (number 18) had no detectible TCDD with a limit of detection of 4 parts per trillion. No specimen was submitted for the assigned number 22.

Table II presents data relevant to the exposure in Vietnam to Herbicide Orange. Group A is composed of the three volunteers (numbers 10, 19, and 26) were judged to be most heavily exposed to the defoliants. Their duties in Vietnam involved handling the chemicals at a time and under circumstances when few precautions were taken to avoid contact or ingestion.

The five veterans comprising Group B are judged to have had relatively little likelihood of exposure to Herbicide Orange either because their location in Vietnam was removed from the areas sprayed (number 1, 15, and 34), because of the time of their Vietnam duty (numbers 13 and 28) or its short duration (number 1), and because of a questionable description of exposure (number 34). The remaining twelve Vietnam veterans appear to have had an intermediate likelihood of exposure, i.e. between that of Groups A and B and are not described in Table II.

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Among the most heavily exposed men are the two (numbers 10 and 26) with the highest TCDD content in their body fat but the other man (number 19) had none detected. Two of the lightly exposed men (numbers 1 and 13) had no detectible TCDD but the other three (numbers 15, 28 and 34) did have.

Table III summarizes the clinical information regarding all twenty Vietnam veterans. Seven of them (numbers 9,13,15,26,27,29, and 30) reported some health problems beginning during a tour of duty in Vietnam. No two, however, reported the same symptoms which included probable numbness and tingling; tingling and swelling of the hands and feet with insomnia due to the pain; plantar warts; a rash on the legs with "jungle rot" and occasional diarrhea; apparently generalized itching; amoebic dysentery as well as pleurisy, weakness, and hypertension; and asthma with cough and an intermittent rash on the flexor surface of the arms. The remaining thirteen veterans reported no illness while in Vietnam although only one reported good health at all times. Among the nineteen veterans with medical complaints six (numbers 1,8,10,19,24, and 26) suffered from conditions difficult to relate to toxic agents, namely malignant astrocytoma; chronic ulcer after laceration of the hand; plantar warts and a "stomach condition" without radiographic or chemical evidence of disease; varicose veins; hemorrhoids, low back pain, and palpable liver with a history of heroin use; and pruritis and possible urticaria. Of the thirteen other veterans reporting difficulties five reported mental problems ranging from nervousness to schizophrenia and three had experienced difficulties of reproduction, namely, spontaneous abortion by the wives of two (numbers 11 and 15) and congenital heart disease in the son of a third (number 16) .

Three of the seven veterans who reported difficulties while in Vietnam had no TCDD detected; the four others had 5 to 96 parts per trillion. Of the six men whose medical complaints were difficult to relate to toxic substances, three had no TCDD and three had 5 to 96 parts per trillion. The category of five veterans with mental problems included two without detectable TCDD and three whose assays results were 5 to 13 parts per trillion. One of three veterans reporting reproductive problems had no detected TCDD and the other two had levels of 3 and 7 parts per trillion.

The lack of relationship between detectable TCDD in the body fat and the usual clinical chemical findings can be illustrated by the fact that none of the men tested had abnormal values for total plasma protein, albumen, thromboplastin, creatinine, or uric acid. The aspartate amino transferase (SGOT) was slightly elevated (21IU/L or less) in three

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veterans without detectable TCDD in their fat and in two with 6 and 35 per trillion. One veteran with an elevation of 48 IU/L and another with an increase of 190 IU/L of SGOT had no TCDD detected. Similar lack of relationship between clinical chemistry and TCDD content is evident for each test.

Summary and Conclusions: As Gross (6) concluded, his method of gas chromatography-mass spectrometry is capable of detecting and measuring very small amounts of TCDD of human fat. The technique is, however, difficult and delicate in its present form. It also requires enough adipose tissue to necessitate surgical biopsy and this must be performed under conditions that avoid contaminating the tissue with TCDD from extraneous sources.

The data indicate that TCDD can be found in some persons who report exposure to Herbicide Orange and in others who were never in Vietnam and know of no contact with the herbicide. On the other hand, some veterans from Vietnam have no detectible TCDD and the same is true of veterans who were never in Vietnam. The low level of TCDD in two Air Force officers and its absence in another is of special interest since their exposure to TCDD is certain and more recent than that of the veterans.

Information regarding pre- and post-service exposure to chemicals that contain TCDD is too inadequate to allow more than speculation on other sources of the material in the fat samples. TCDD has been found in a substance other than Herbicide Orange or the 2,4,5-T in that mixture (1). It is impossible, therefore, to be certain of the source of TCDD found in any of the men in this study.

Because of the difficulty and limited availability of the assay techniques, the necessity for securing relatively large fat samples, and the uncertainty of the source of the TCDD detected, the method described here does not seem a satisfactory routine test for exposure to Herbicide Orange nor acceptable evidence of contact with that specific defoliant nor of the absence of such contact. It will provide a research tool under proper conditions and for specific purposes, e.g. the study of the rate of disappearance of TCDD after known exposure.

It should be noted that the amounts of TCDD measured in the fat are very small, not exceeding 100 parts per trillion. Since the substance is more concentrated in fat than in other tissues, the total body concentration is even less.

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- (6) Gross, M.L. 1980. Trace analysis of tetrachlorodibenzo-p-dioxin (TCDD) in human adipose in publication.

Table I. TCDD in Human Fat Samples (after Gross (6))

Veterans with Military Service in Vietnam

Subject	TCDD Presence	TCDD Concentration ^a (parts per trillion)	
		<u>m/z</u> 392: <u>m/z</u> 328	<u>m/z</u> 322
1	Neg. ^b	nd (11) ^c nd (5)	- ^d
6	Neg. ^b	5 (3) -	2 nd
8	Neg. ^b	5 (3) -	2 nd
9	Neg. ^e	nd (12) nd (3) nd (4)	- - 1
10	Pos.	12 (2) 16 (4) 35 (9) 23 (4)	- - 21 17
11	Pos.	3 (2) -	2 1
12	Pos.	9 (3)	13
13	Neg.	nd (2) nd (2)	- -
14	Doubtful ^f	4 (3)	4
15	Pos.	7 (4)	8
16	Neg.	nd (4) nd (8)	- -
19	Neg.	nd (15) nd (3)	- -
24	Pos.	5 (4) 5 (3)	- 3
25	Pos.	12 (4) 10 (3)	- 11
26	Pos.	63 (6) 96 (10)	- 100

27	Neg.	nd (11) nd (6)	- nd
28	Pos.	8 (6) 7 (5)	3
29	Pos.	nd (6) 13 (5)	- 8
30	Neg.	9 (4) nd (3)	- nd
34	Pos.	4 (4) 5 (3)	- (5)

Air Force Officers

2	Pos.	5 (2)	4
3	Neg. ^b	4 (1)	2
4	Pos.	6 (6)	4

Veterans with Military Service Outside Vietnam

5	Neg. ^b	9 (5) 4 (4)	6 5
7	Neg. ^e	3 (2)	2 nd
17	Doubtful	3 (3) 4 (3)	2 3
18	Neg.	nd (4)	-
20	Pos.	5 (4)	5
21	Neg. ^e	6 (3)	2
23	Pos.	6 (3) 8 (2)	- 8
31	Neg. ^e	4 (2)	-
32	Doubtful	nd (5) 4 (4)	- 5
33	Neg. ^e	7 (6) 14 (7)	- 5

4. 2
- a. m/z 322: m/z 328" is value calculated from relative signal intensities at two mass spectrophotometer channels. " m/z 322" is value from absolute intensity of that channel.
- b. Cannot be considered positive because of poor validation (substance detected probably not TCDD) and contaminant removed on repeat analysis.
- c. "nd" means "not detectable". Value in parentheses is limit of detection of TCDD.
- d. Dash indicates no assay performed.
- e. Cannot be considered positive because of poor validation (substance detected probably not TCDD).
- f. "Doubtful" indicates that result would be considered positive at 2.5:1 signal: noise ratio negative at 3:1 ratio.

Table III. SUMMARY OF CLINICAL INFORMATION

SUBJ:	Age	Civilian Occupation	Non-Service Exposures	Immediate Symptoms	Intermediate Health	Current Symptoms	Current Positive Findings	Diagnoses	Comments
1	31	Well Maintenance on disability	Chlorine; Chemo-therapy, radiation	None given	Lt. temporo-parietal tumor; "kidney condition"	None	None	Malignant astrocytoma - 1976	
6	31	Machine Keeper	Radiation - tonsils 1950	None given	Acoustic neuroma	Headaches - 1 1/2 yrs Facial pain	Thyroid nodule, facial N. changes	Acoustic neuroma-1979, thyroid nodule 1976	
8	30	Construction-unemployed	None - ETOH, cocaine, marijuana use	None given	No reported difficulty	Ulcer-after cut - 2-3 mon.	Ulcer - L index finger	Chronic ulceration	
9	30	Student	None	? Numbness & tingling	Rhinitis, "back condition" - 1969	Numbness, tingling fatigability, fever-yrs. "Psychiatric & sexual problems"	Hostile - abdominal tenderness, pharynx edema	None	
10	30	Steel mill crane operator; student	None	None given	Back pain, Chr. otitis media, plantar wart	"Stomach condition"	None	Plantar wart	
11	32	Student; Construction worker	None	None given	Wife aborted at 3-4 mon - 2 1/2 years ago	Intermittent chest pain & dyspnea - 2 yrs Urinary frequency - 2 yrs., Infertility	None	None	
12	30	Technical representative for Clinical Instru. Company	None	None given	Butterfly facial rash after ETG; or anxiety - before Vietnam as well	None	Butterfly rash on face & forehead		

AP 0144

SUMMARY OF CLINICAL INFORMATION

SUBJ:	Age	Civilian Occupation	Non-Service Exposures	Immediate Symptoms	Intermediate Health	Current Symptoms	Current Positive Findings	Diagnoses	Comments
13	29	School Teacher	(TP4 in service) Heroin for 3 yr 4 yr. ago	Plantar warts	Mastectomy for bynecomastia - 1974	200X swollen lids & red conjunctiva; nervousness, tingling of fingers & toes - "several years", periodic weakness	Jumpy, small non-tender axillary nodes	none	
14	32	Construction	Farm chemicals; photographic; lawn fertilizer	None given	Kidney stone-1975; Pleurisy & pneumonia 2 wks; PPD pos.- 1969; blood in stools	Chestpain; forehead cyst; lipoma, mole, hernia	Prominent hila, disc atelectasis	Sarcoidosis, inguinal hernia lipoma cyst	
15	33	Machine repair- man	Cleaning agents heavy ETOH	Rash on legs; occasional diarrhea; jungle rot of toe-nails & groin	Nervousness-late 1972; wife aborted 1X between 1969 & 1975; "nervous breakdown"-1972	Recurrent extremity welling-10 yrs., "nerves", rash	Pigmented areas on lt. thigh and lower legs	Schizophrenia. skin rash, cnychomycosis	
16	35	Piper fitter	None	None given	Son-congenital heart dis. 1971	Dry cough-3 wks., foot problems-since service	Lt. great toe contract ure; tenia pectis	none	
19	51	Machinist (?)	None	None given	No Statement	Painful leg edema	Varicose veins	Varicose veins	
24	33	Tailor	None. Heroin- until 3 yr. ago	None given	Painful knee & leg swelling after exercise	Groin pain - few yrs. low back pain	Hemorrhoids; Palpable liver	hernia	
25	34	Auto Mechanic	Insecticides	None given	Recurrent dry patches on back & shoulders; peptic ulcer	Pain, swelling left knee-post-traumatic	BP 150/100; arthoscopy cholecystectomy, tenia versicolor	Arthritis, chronic chole- cystitis, fatty liver, HBP,	

AP 0145

SUMMARY OF CLINICAL INFORMATION

SUBJ:	Age	Civilian Occupation	Non-Service Exposures	Immediate Symptoms	Intermediate Health	Current Symptoms	Current Positive Findings	Diagnoses	Comments
26	33	Artist	None	None given	Crampy abdominal pain-4 yr. ago; allergy to fish & IVP dye	Severe rectal itch-3 yr; generalized skin itch occasionally since 1968	Perianal excoriated lesion	Pruritis ani, Possible urticaria	
27	32	None given	None	None but tingling & swelling of hands & feet insomnia from pain	Still fingers & toes Hematemesis; back pain	Reynaud -like reaction & weakness of extremities	Stiff fingers & toes, bilateral limp	none	
28	33	MAS (VA)	None	None given	None	None	None	None	
29	30	Carpenter	None	None given	Amoebic dysentery; pluerisy 2 mon in Vietnam; "weak" before discharge; HBP at discharge; Crampy abd. pain-1976' "Poly cystic kidney"	Early morning weakness normal by evening	None BP 158/90	Duodenitis	
30	30	Oil Tank leader Fireman	Primary light oils-benzene, toluene, etc.	Repeated cough, asthma worse (t. evac. hos)	Nervousness	Intermittent pruritic rash on flexor surface of arms-since Vietnam	Expiratory rhonchi	None	
34	37	Carpenter	None	None Given	Multiple, generaliz-ed lipomata	Chr. anxiety, dyspnea blurred vision; palpitations; chest pain, stomach pain; facial flushing, infraorbital "water blisters" 1 each week, HBP	Abdominal nodules (lipomata ?)	None	

AP 11 6196

SUMMARY OF CLINICAL INFORMATION

SUBJ:	Ag	Civilian Occupation	Non-Service Exposures	Immediate Symptoms	Intermediate Health	Current Symptoms	Current Positive Findings	Diagnoses	Comments
2	38	USAF	Farm defolianta	None	None	None	Mass (?) left axilla		
3	36	USAF	Laborat. insecticides	None	Bronchiectasis, penicillin allergy	None	None		
4	39	USAF	Organo-phosphates, industrial HCOs	None	NCC arthritia, renal stone, spastic colon	Occasional periorbital acne-3yrs., mole-like lesions of arm, groin, penis	None	None	
5	34	Unemployed	No record	Not applicable	None given	None given	Rt. inguinal hernia	Hernia	
7	40	Unemployed	No record	Not applicable	None given	None given		Rectal adenocarcinoma	
17	31	Not reported	Gasoline & automotive chemicals	Not applicable	Pelvic fractions	Acute low back pain. Infertility (past pelvic fracture)	Rt. varicose vv.; Rt. leg atrophy; Lumbar spasm	Epigastric hernia, acute lombosacral sprain	
18	51	Not recorded	Not given	Not applicable	HBP, allergy to dyes	Intermittent hematuria-9mon.	Calculus-rt. kidney	Rt. renal calculus Hypertension	Ureterolithotomy
20	48	Not recorded	Not given	Not applicable	"Back problems" gout-12 yrs. ago	Severe abdominal & back pain	Sliding hiatal hernia; ureteral	Ureterolithiasis; Hypertension	Ureterolithotomy
21	43	Federal Employee	None	Not applicable	Not recorded	Known non-functioning kidney	None	Rt., non-functioning, multicystic kidney	Nephrectomy

AP 6147

SUMMARY OF CLINICAL INFORMATION

SUBJ:	Age	Civilian Occupation	Non-Service Exposures	Immediate Symptoms	Intermediate Health	Current Symptoms	Current Positive Findings	Diagnoses	Comments
23	31	Foreman meat cutter	None given	Not applicable	Duodenal ulcer, bronchial asthma	Exigastric pain, vomiting-1/2 yr	Obesity	Hiatus hernia & reflex esophagitis, asthma	Nissen fundoplication
31	27	Sheet-metal machine operator	None, drug abuse	Not applicable	Automobile accident with right hip injury	Hip pain	Limit movement, rt. hip. Abscess mandible	Traumatic dislocation rt. hip; osteonecrosis; anemia	Hip fusion
32	43	Retired AF and Marine	None	Not applicable	Dermatitis, left foot; arthritis chest & left arm pains, dyspnea 6-7yrs	Sinus headaches, tics	Bilat, direct inguinal hernia Hemorrhoids	Left inguinal hernia	Herniorrhaphy
33	42	Manager-auto repairs	None given	Not applicable	None given	None given	None given	Cholelithiasis	Cholecystectomy