

## DIOXIN AND DIBENZOFURAN ELEVATION IN HUMANS FOLLOWING EXPOSURE: YUSHO, AGENT ORANGE EXPOSED VIETNAMESE, A PHENOXY-HERBICIDE EXPOSED AMERICAN VETERAN WITH SOFT TISSUE SARCOMA, AND CHLOROPHENOL EXPOSED AGRICULTURAL WORKERS FROM CHINA

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**Objective:** Congener-specific dioxin (PCDD) and dibenzofuran (PCDF) tissue levels are reported from four case studies involving occupational or environmental contamination. The first is from the Yusho rice oil poisoning in Japan which occurred in 1968; blood taken from four patients two decades after exposure will be analyzed and the individual values reported. The second is Vietnam, where the phenoxyherbicide Agent Orange (contaminated with 2,3,7,8-TCDD) was sprayed between 1962 and 1970; pooled blood of over 2,000 adults from over 20 affected locations has been collected and mean levels of pooled samples are compared with control blood specimens from the north of Vietnam. The third case report is of a herbicide-exposed American veteran who subsequently developed soft tissue sarcoma, a cancer which caused his death. We report blood, liver and adipose tissue PCDD/Fs, noting tissue partitioning in this patient who was suffering cachexia (wasting) due to cancer. Fourth, pentachlorophenol (PCP) exposed agricultural workers from a middle China province where PCP was used for insect control are compared with general population blood from the People's Republic of China.

**Methods:** The Yusho blood was obtained in 1990 and 1991, over two decades after the exposure, which occurred in 1968. The Vietnamese blood was obtained at regional hospitals from samples drawn for other purposes that would normally be discarded at the end of each day. The blood from the veteran was obtained in 1991, shortly before his death, whereas liver and adipose tissue were obtained by autopsy. The Chinese blood was obtained in 1993. All

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samples were frozen immediately after collection and kept frozen until dioxin analysis was performed. The analytic methods were those used by the dioxin laboratory<sup>1</sup> in its successful participation and "certification" in recent WHO interlaboratory validation studies on human tissues, and will not be repeated.<sup>2</sup>

**Results:** Representative data from 433 patients' from southern Vietnam, 183 patients from central Vietnam, and 82 patients from the non-Agent Orange sprayed north of Vietnam are presented in Table I. Blood was obtained approximately 20 years after Agent Orange spraying ended from the south of Vietnam. Contrast between the higher average 2,3,7,8-TCDD levels of 12.9 and 13.2 ppt lipid in south and central Vietnam and the lower 2.2 ppt level in the north can be noted. Lower dioxin and dibenzofuran congener levels characteristic of the less industrial north can be noted also. More detailed information, by individual district and village levels, will be presented at Dioxin '93.

Table II presents dioxin and dibenzofuran congener data, on a lipid normalized basis, from whole blood, adipose tissue, and liver tissue of an American veteran previously exposed to a phenoxyherbicide believed to be Agent Orange. The veteran was diagnosed as having soft tissue sarcoma, a cancer sometimes associated with dioxin exposure. TCDD levels are similar at 19, 16 and 13 ppt lipid in blood, fat tissue and liver, respectively. OCDD levels are 957, 1975 and 1969, respectively. Total dioxin toxic equivalents (TEQ) are 66, 99 and 78 ppt, respectively. Individual congener partitioning for each tissue is also presented in Table II. We and others have previously published partitioning data in 20 matched blood and adipose specimens which show that 2,3,7,8-TCDD levels are similar on a lipid basis in blood and adipose tissue, unlike the higher chlorinated congeners, which are higher in blood.<sup>3</sup>

The Yusho blood is being analyzed at this time, we expect the results to show high TEQ values due to high levels of 2,3,4,7,8-PnCDF and 1,2,3,4,7,8-HxCDF from the patient's ingestion of contaminated rice oil. Data will be presented for the four patients at Dioxin '93. The Chinese blood is being processed at the time of manuscript preparation.

**Conclusions:** The Vietnamese data show that although Agent Orange spraying began in 1962 and ended in 1970, TCDD elevation still persists in humans at varying levels in these samples collected between 1988-91. The partitioning of dioxins and dibenzofurans in the veteran's tissues is of interest because of the lack of data concerning tissue levels of dioxins in patients with wasting syndromes as seen with cancer, AIDS, or some infectious diseases. Further research is needed to address the question of interpretation of tissue levels as a reflection of body burden under these circumstances.

## References:

- 1 Pöpke O, Ball M, Lis ZA, Scheunert K. Determination of PCDD/PCDF in whole blood from persons involved in fire incidents. *Chemosphere* 1990;20:7/9:959-966.
- 2 World Health Organization. *Levels of PCBs, PCDDs and PCDFs in human milk and blood: Second round of quality control studies - Environment and Health in Europe #37*. Denmark: FADL Publishers, 1991;1-76.
- 3 Schecter AJ, Ryan JJ, Constable JD, Baughman R, Bangert J, Fürst P, Wilmers K, Oates RP. Partitioning of 2,3,7,8-chlorinated dibenzo-p-dioxins and dibenzofurans between adipose tissue and plasma lipid of 20 Massachusetts Vietnam veterans. *Chemosphere* 1990;20:1/7:951-958.

**TABLE I: MEAN PCDD/F VALUES AND DIOXIN TOXIC EQUIVALENTS FOR POOLED VIETNAMESE BLOOD BY GEOGRAPHIC REGION (ppt, lipid)**

Congener	TEF*	South N=433	TEq†	Central N=183	TEq	North N=82	TEq
<b>Dioxins (PCDDs)</b>							
2,3,7,8-TCDD	1	12.9	12.9	13.2	13.2	2.2	2.2
1,2,3,7,8-PeCDD	0.5	8.0	4.0	16.3	8.2	4.1	2.1
1,2,3,4,7,8-HxCDD	0.1	6.6	0.7	13.0	1.3	3.7	0.4
1,2,3,6,7,8-HxCDD	0.1	29.9	2.9	46.2	4.6	13.4	1.3
1,2,3,7,8,9-HxCDD	0.1	8.3	0.8	13.4	1.3	4.8	0.5
1,2,3,4,6,7,8-HpCDD	0.01	77.2	0.8	78.1	0.8	25.5	0.3
OCDD	0.001	616.1	0.6	751.0	0.8	132.1	0.1
<b>Dibenzofurans (PCDFs)</b>							
2,3,7,8-TCDF	0.1	2.1	0.2	2.9	0.3	4.6	0.5
1,2,3,7,8-PeCDF	0.05	1.8	0.09	2.2	0.1	1.7	0.09
2,3,4,7,8-PeCDF	0.5	8.3	4.2	14.9	7.5	7.6	3.8
1,2,3,4,7,8-HxCDF	0.1	21.1	2.1	67.4	6.7	20.6	2.1
1,2,3,6,7,8-HxCDF	0.1	13.0	1.3	40.0	4.0	11.1	1.1
1,2,3,7,8,9-HxCDF	0.1	0.7	0.1	0.7	0.1	0.5	0.1
2,3,4,6,7,8-HxCDF	0.1	2.3	0.2	3.0	0.3	2.2	0.2
1,2,3,4,6,7,8-HpCDF	0.01	37.8	0.4	75.7	0.8	46.7	0.5
1,2,3,4,7,8,9-HpCDF	0.01	3.4	0.03	1.9	0.02	1.9	0.02
OCDF	0.001	3.9	0.004	5.1	0.005	4.2	0.004
<b>TOTAL PCDDs</b>		<b>759</b>	<b>22.7</b>	<b>931</b>	<b>30.2</b>	<b>186</b>	<b>6.9</b>
<b>TOTAL PCDFs</b>		<b>94</b>	<b>8.6</b>	<b>214</b>	<b>19.8</b>	<b>101</b>	<b>8.4</b>
<b>TOTAL PCDD/Fs</b>		<b>853</b>	<b>31.3</b>	<b>1145</b>	<b>50</b>	<b>287</b>	<b>15.3</b>

\* Dioxin Toxic Equivalency Factors

† Dioxin Toxic Equivalents

**TABLE II: BLOOD, ADIPOSE TISSUE, AND LIVER DIOXIN AND DIBENZOFURAN LEVELS FROM AN AMERICAN VETERAN WITH TERMINAL SOFT TISSUE SARCOMA AND WASTING (ppt, lipid)**

Congener	TEF*	Blood	TEq	Adipose	TEq	Ratio Adipose/ Blood	Liver	TEq	Ratio Liver/ Blood
2,3,7,8-TCDD	1	19	19	16	16	0.84	13	13	0.68
1,2,3,7,8-PeCDD	0.5	19	9.5	39	19.5	2.05	29	14.5	1.53
1,2,3,4,7,8-HxCDD	0.1	27	2.7	29	2.9	1.07	20	2	0.74
1,2,3,7,8,9-HxCDD	0.1	22	2.2	22	2.2	1.0	15	1.5	0.068
1,2,3,6,7,8-HxCDD	0.1	147	14.7	303	30.3	2.06	196	19.6	1.33
1,2,3,4,6,7,8-HpCDD	0.01	133	1.3	190	1.9	1.43	150	1.5	1.13
OCDD	0.001	957	0.96	1975	2.0	2.06	1969	2.0	2.05
2,3,7,8-TCDF	0.1	1.8	0.18	3.4	0.34	1.89	2.4	0.24	1.33
2,3,4,7,8-PeCDF	0.5	19	9.5	34	17	1.79	28	14	1.47
1,2,3,7,8,-PeCDF	0.05	ND(1)	0.03	ND(1)	0.03	1.0	ND(1)	0.03	1.0
1,2,3,4,7,8-HxCDF	0.1	37	3.7	38	3.8	1.03	54	5.4	1.46
1,2,3,7,8,9-HxCDF	0.1	ND(1)	0.03	ND(1.2)	0.06	1.2	ND(1)	0.05	1.0
1,2,3,6,7,8-HxCDF	0.1	16	1.6	20	2	1.25	33	3.3	2.06
2,3,4,6,7,8-HxCDF	0.1	1.9	0.19	2.1	0.21	1.11	1.2	0.12	0.63
1,2,3,4,6,7,8-HpCDF	0.01	34	0.34	53	0.53	1.56	73	0.73	2.15
1,2,3,4,7,8,9-HpCDF	0.01	ND(2.8)	0.01	1.9	0.02	1.36	12	0.12	8.57
OCDF	0.001	ND(4.2)	0.002	3.1	0.001	NA	4.1	0.004	NA
TOTAL PCDDS		1324	50	2574	75		2392	54	
TOTAL PCDFS		114	16	157	24		209	24	
TOTAL PCDD/Fs		1438	66	2731	99		2601	78	
% LIPID		0.38		50.0			5.0		

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