Concentrations of PCDDs and PCDFs in Human Tissue 36 Years after Accidental Dioxin Exposure

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Introduction: On 17 November 1953, an uncontrolled decomposition reaction occurred in an enclosed production facility at BASF, Ludwigshafen. Dioxins were formed during the reaction and contaminated the autoclave section of the building. Employees were exposed to the dioxin contaminants during subsequent cleanup and repair activities. Both morbidity and mortality followup studies of exposed employees have been conducted and reported over the years, most recently in 1990[1]. Since the closing date of the most recent mortality update (12/31/87), several additional members of the cohort have died. For three individuals whose deaths were due to cancer, autopsy material was obtained for quantitative PCDD and PCDF analysis. In a fourth living case, tissue specimens were available following surgery for a liver carcinoma.

Subjects and Methods: The four individuals, for whom tissue specimens were obtained, had all been included in the prior mortality study. The first individual (case 1) was a mechanic who performed cleanup work after the accident for one week in December 1953 and subsequently developed severe chloracne. He died in May 1989 at the age of 69 from acute myelogenous leukemia. The second subject (case 2) was an assistant plant supervisor of a neighboring plant who was assigned shift work in the accident building for a few days in December 1953. He was diagnosed with mild chloracne. This employee died in July 1990 from bronchogenic carcinoma at age 66. His 2,3,7,8-TCDD blood level five months prior to death was 17 ppt. The third person (case 3) was a fireman who entered the autoclave room for brief cleanup work within hours of the accident. He was never known to have developed chloracne. He was diagnosed with pancreatic carcinoma and died in December 1989 at the age of 80. His 2,3,7,8-TCDD blood level eight months prior to death was 518 ppt. The last employee (case 4) was a mechanic who took part in cleanup activities beginning one day after the accident. He developed chloracne of one year's duration. In 1988 at age 58, he was diagnosed with carcinoma of the liver; he has undergone operations in 1988 and 1991, respectively. His 2,3,7,8-TCDD blood level from 1989 was 553 ppt.

Tissue samples of 20-50 grams were collected during autopsy in specially prepared test tubes provided by ERGO Forschungsgesellschaft, Hamburg. The samples were deep frozen and transported by express to the laboratory for analysis. The ERGO laboratory successfully participated in the 1990 WHO PCDD/F interlaboratory quality assurance program. PCDDs and PCDFs were determined on a lipid basis from 10-20 gram homogenized tissue samples spiked with commercially available 13-C-labelled internal quantification standards.

The measurements were performed by gas chromatography/mass spectroscopy on DB5 fused silica columns using a VG 7035 or VG AutoSpec-system at a mass resolution of 2,000 or 10,000, respectively.

Results: Compared to an average "background" concentration of 5 ppt for unexposed individuals, case 1 shows a 40 to 50-fold increase in 2,3,7,8-TCDD for all tissues except the brain (see Table 1). In general, PCDD and PCDF concentrations expressed on a lipid weight basis, did not vary between blood, adipose tissue and kidneys and were not elevated relative to background except for 2,3,7,8-TCDD. Concentrations of the higher chlorinated dioxins and furans were much greater in the liver. This same pattern with respect to the liver was observed across all cases.

For case 2, a six-fold increase in 2,3,7,8-TCDD level was observed relative to background (Table 2). Again the concentrations of all PCDDs and PCDFs were relatively lower in brain. During the last five months of life, blood levels of 2,3,7,8-TCDD increased from 17 to 32 ppt. This was most likely a consequence of adipose tissue loss due to illness; the patient was known to have lost 7 kgs in the last months of life alone.

Concerning case 3, blood levels of 2,3,7,8-TCDD were considerably higher (518 ppt) eight months prior to death in this 80 year-old individual with pancreatic cancer (Table 3). A further 14-fold increase in 2,3,7,8-TCDD blood level was observed at death. This was probably due to extreme weight loss associated with cancer cachexia. A heavily reduced fat content of all respective tissues was described in the autopsy report, so it was not possible to obtain any post mortem adipose tissue. The cachexia that occurred must be taken into account in evaluating the PCDD and PCDF concentrations found in various tissues.

The increased blood concentrations of PCDDs and PCDFs associated with cachexia over an eight month period are shown in Table 4. The concentrations range from 6 to 25 times higher at death depending on congener. The liver concentrations of the higher chlorinated PCDDs and PCDFs are also remarkable in this individual.

The PCDD and PCDF congener concentrations in brain relative to blood lipids are presented for case 3 in Figure 1. These comparisons show that the relative level of dioxins and furans in brain tissue declines with increasing degree of chlorination. A similar pattern is seen with cases 1 and 2.

Case 4: Dioxin levels of liver, adipose tissue and blood will be presented. The results of these samples are not yet available at the time of submission of this manuscript.

Discussion and Summary: Recently published PCDD/F concentrations of some SID (sudden infant death) samples (liver, brain, adipose tissue)[5] fit well with our observations of the distribution between the organs of question.

In this report we present tissue PCDD and PCDF concentrations for four individuals up to 36 years after known 2,3,7,8-TCDD exposure. Our results can be summarized as follows:

- 2,3,7,8-TCDD blood concentrations correlated well those of other tissues when expressed on a lipid weight basis,
- higher chlorinated PCDD and PCDF congeners are more likely to be found in liver tissue and less likely to be found in brain tissue relative to the lower chlorinated congeners,
- during severe weight loss, lipid-adjusted PCDD and PCDF concentrations may increase by more than an order of magnitude; even higher relative concen-

trations may be found in liver tissue,

- on a lipid adjusted basis, the lowest concentrations of PCDDs and PCDFs are found in brain tissue.

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Case 1: Pre autopsy blood level not available

	Sample					German "background" concentrations in adipose tissue: mean values [2,3,4]
	Blood	Adipose tissue	Liver	Kidney	Brain	
2,3,7,8 Tetra-CDD	255	171	178	198	36	5
1,2,3,7,8 Penta-CDD	20	9	16	8	<0.5	20
$\sum$ Hexa-CDD	92	60	168	64	0.8	121
1,2,3,4,6,7,8 Hepta-CDD	60	23	794	159	<0.4	124
Octa-CDD	436	389	6098	592	2.8	633
2,3,7,8 Tetra-CDF	3.2	0.6	3.4	<2	n.d.	3
$\sum$ Penta-CDF	54	47	343	64	1	47
$\sum$ Hexa-CDF	48	19	838	42	0.5	45
$\sum$ Hepta-CDF	17	3	247	5	n.d.	21
Octa-CDF	n.d.	<1	7	n.d.	n.d.	4
TEQ (BGA)	278	185	331	218	36	30
I-TEQ (NATO / CCMS)	308	207	474	247	37	50

Table 1 PCDD and PCDF concentrations in pg/g (ppt) based on extractable fat content of various autopsy tissues

Case 2: 2,3,7,8 TCDD blood level 5 months prior to death: 17 ppt

	Sample					German "background" concentrations in adipose tissue: mean values [2,3,4]
	Blood	Adipose tissue	Liver	Bone marrow	Brain	
2,3,7,8 Tetra-CDD	32	34	28	32	7	5
1,2,3,7,8 Penta-CDD	32	24	24	23	1	20
$\sum$ Hexa-CDD	77	66	81	66	1	121
1,2,3,4,6,7,8 Hepta-CDD	25	18	174	17	0.1	124
Octa-CDD	262	257	2781	240	13	633
2,3,7,8 Tetra-CDF	<5	0.8	1	0.9	0.3	3
$\sum$ Penta-CDF	27	29	99	33	1	47
$\sum$ Hexa-CDF	22	16	170	14	0.5	45
$\sum$ Hepta-CDF	31	14	239	12	0.7	21
Octa-CDF	-	0.7	5	n.d.	n.d.	4
TEQ (BGA)	49	48	73	47	7	30
I-TEQ (NATO / CCMS)	71	69	121	69	8	50

Table 2 PCDD and PCDF concentrations in pg/g (ppt) based on extractable fat content of various autopsy tissues

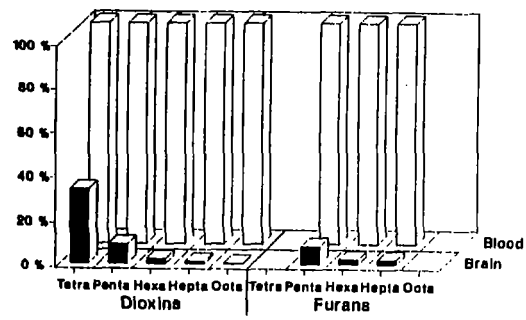
Case 3: 2,3,7,8 TCDD blood level 8 months prior to death: 518 ppt						
	Sample					German "background" concentrations in adipose tissue: mean values [2,3,4]
	Blood	Liver	Kidney	Pancreatic tumor	Brain	
2,3,7,8 Tetra-CDD	7482	15563	11195	13523	2457	5
1,2,3,7,8 Penta-CDD	220	1001	346	464	19	20
∑ Hexa-CDD	1255	14889	1829	3177	29	121
1,2,3,4,6,7,8 Hepta-CDD	604	55602	930	2068	7	124
Octa-CDD	9755	424395	5876	12652	41	633
2,3,7,8 Tetra-CDF	<2.5	6.5	4	2.2	0.4	3
∑ Penta-CDF	487	17930	888	1156	39	47
∑ Hexa-CDF	261	27768	368	496	6	45
∑ Hepta-CDF	77	9477	68	141	1.6	21
Octa-CDF	n.d.	231	n.d.	14	1.2	4
TEQ (BGA)	7721	20798	11554	14087	2467	30
I-TEQ (NATO / CCMS)	8002	28345	12048	14734	2488	50

Table 3 PCDD and PCDF concentrations in pg/g (ppt) based on extractable fat content of various autopsy tissues

	Concentrating factor
2,3,7,8 Tetra-CDD	14
1,2,3,7,8 Penta-CDD	25
∑ Hexa-CDD	19
1,2,3,4,6,7,8 Hepta-CDD	5.5
Octa-CDD	8.6
2,3,7,8 Tetra-CDF	-
∑ Penta-CDF	2.2
∑ Hexa-CDF	6.1
∑ Hepta-CDF	4.1
Octa-CDF	-
TEQ (BGA)	14

Table 4 Concentrating factors for PCDDs and PCDFs in two blood samples of a tumor patient during cachexia within 8 months (case 3)

Figure 1 PCDD / PCDF - Relationship Blood Lipids/Brain-Extractables



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