PCDDs and PCDFs in Blood from Swedish Phenoxy Herbicide Workers

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Abstract

Blood samples from five Swedish male workers in a phenoxy herbicide plant were analyzed for PCDDs, PCDFs and non-ortho PCBs together with blood from five male reference persons. The workers had much higher concentrations of 2,3,7,8-tetra CDD than the referents. A relationship was found between the employment time and the blood levels. Most other PCDDs, PCDFs and PCBs were also higher in the workers than in the referents. Especially the concentration of 1,2,3,7,8-penta CDD was much higher in the workers than in the reference group, which was completely unexpected.

Introduction

In Sweden there was considerable legal and public commotion in the late 1970s concerning a factory in southern Sweden producing roughly 2 000 tons/year of chlorophenoxy herbicides including esters of 2,4,5-trichlorophenoxy acetic acid (2,4,5-T), 2,4-D, 2,4-DP, MCPA and MCPP as well as about 200 tons/year of 2,4,6-trichlorophenol via direct chlorination of phenol. The phenoxy esters were prepared in a reaction between the corresponding chlorophenate and monochloroacetate. The starting material 2,4,5-trichlorophenol was imported, primarily from Germany; no production took place at the site.

The surrounding environment was polluted, and there was concern about possible harm to the health of the workers and the general population. One of the main issues was the potential exposure to 2,3,7,8-tetra CDD, which is a known by-product formed during the synthesis of 2,4,5-trichlorophenol. Although a quantity of 80 μg/ kg of 2,3,7,8-tetraCDD was detected in waste barrels and two 2,4,5-T formulation from the factory from the 1972 production contained 30 and 70 μg/kg of 2,3,7,8-tetra CDD respectively, the conclusion at that time was that there had been no significant exposure to 2,3,7,8-tetra CDD.

There is some epidemiological evidence on the carcinogenicity of chlorophenoxy herbicides and chlorophenols. However, the question of causative agent(s) - the pesticides

themselves and/or the contamination by PCDDs and/or PCDFs awaits solution. Thus a cohort of 270 workers from the above mentioned factory has been followed as part of an international cohort maintained by the International Agency for Research on Cancer, IARC (1).

Materials and Methods

Blood samples were drawn from five male workers in the above mentioned factory and five referents. Workers and referents were comparable in age (workers average 63, range 43 - 75; referents average 63, range 43-70 years), social status, site of living, body mass index, fish consumption and smoking habits. The blood plasma was separated from the red cells and the coded plasma samples were shipped to the analytical laboratory, the exposure status was unknown to the analytical chemists. The samples were analyzed for PCDDs, PCDFs and non-*ortho* PCBs using analytical methods validated in international intercalibration studies (2,3). The analyses of PCDDs and PCDFs included all 2,3,7,8-substituted congeners, tetra through octachlorinated. The PCB analyses included IUPAC numbers 77, 126 and 169.

Results

The results are collected in Table 1, where the means, the ranges as well as the Wilcoxan's p-values are given for the 17 2,3,7,8-substituted PCDDs and PCDFs and the non-*ortho* PCB congeners 77, 126 and 169. Included are also the toxic equivalent figures excluding and including the PCBs.

Discussion

The blood of the workers had much higher concentrations of 2,3,7,8-tetra CDD than the referents. Further, although 16-21 years had passed since the workers left employment, there was an exposure-concentration relationship between the employment time (mean 109, range 83-150 months) and the concentrations of 2,3,7,8-tetra CDD found ($r_S = 0.9$; $p = 0.05$). These concentrations of 2,3,7,8-tetra CDD are the highest found in Sweden, even above those found in fishermen with extensive consumption of fatty fish from the Baltic Sea contaminated by PCDDs, PCDFs and PCBs (4). These concentrations are comparable to the concentrations observed in some other factory workers (5,6), Vietnam veterans 15-20 years after the exposure in Vietnam (5,7) and pesticide sprayers (5). At the end of the employment, the concentration of 2,3,7,8-tetra CDD in the present workers must have been even higher. Assuming a biological half-life of 7.1 or 11.3 years (8, 9) the concentrations then should have been 82 (37-177) or 45 (21-98) pg 2,3,7,8-tetra CDD/g extracted fat respectively. Surprisingly, most other PCDDs, PCDFs as well as the non-*ortho* PCBs, especially IUPAC 126, were

also higher in the workers than in the referents. In term of Toxic Equivalents (I-TEF) the present workers had concentrations in the range of the Baltic Sea fisherman (4). A very probable source of the 2,3,7,8-tetra CDD was the 2,4,5-trichlorophenol, but the source of the other 2,3,7,8-substituted PCDDs and PCDFs is unknown.

It is interesting to note that the observed concentrations of 1,2,3,7,8-penta CDD for the workers are higher than the observed concentrations of 2,3,7,8-tetra CDD, and also significantly higher than the value found for the referents ($p = 0.008$). This is unexpected, since exposure to 2,4,5-T or 2,4,5-trichlorophenol has so far been associated with increased concentrations of 2,3,7,8-tetra CDD only. The source of 1,2,3,7,8-penta CDD is unclear. One possibility could be the on site production of 2,4,6-trichlorophenol or pentachlorophenol, which was not intentionally produced but this compound has been found in environmental samples from the factory and its surroundings. Another possibility could be the use of sodium hypochlorite in the synthesis of 2,4,5-T from 2,4,5-trichlorophenol (10). The observation of increased blood levels of 1,2,3,7,8-penta CDD could be correlated to an analysis of a leachate from the factory taken in 1992. In this sample we found a concentration of 2,3,7,8-tetra CDD of 160 pg/m^3, while the concentration of 1,2,3,7,8-penta CDD was as high as 700 pg/m^3.

The concentrations of PCBs were also found to be higher in the workers as compared to the referents. This is in agreement with PCB concentrations as high as 13% in some barrels found in the factory. It is evident that PCB was used in some part of the production.

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Table 1. Blood plasma concentrations of dioxins/dibenzofurans/non-ortho-PCBs (IUPAC) in five phenoxy herbicide/chlorophenol production workers and five referents.

Analyte	Plasma concentration (pg/g extracted fat) Workers Mean&	Range	Referents Mean&	Range	p*
Dioxins					
2,3,7,8-TCDD	17	9.1-37	2.0	0.7-3.3	0.008
1,2,3,7,8-PeCDD	22	14-33	6.9	4.0-10	0.008
1,2,3,4,7,8-HxCDD	4.5	2.7-6.9	2.4	0.8-4.4	0.2
1,2,3,6,7,8-HxCDD	43	28-58	28	10-39	0.2
1,2,3,7,8,9-HxCDD	18	8.8-27	7.5	2.0-13	0.1
1,2,3,4,6,7,8-Hp-CDD	87	33-120	43	7.9-78	0.06
OCDD	750	400-1300	280	110-440	0.02
Dibenzofurans					
1,2,3,7,8-PeCDF	0.34	<0.2-1.3	0.42	<0.2-1.0	0.5
2,3,4,7,8-PeCDF	34	13-57	20	6.3-33	0.2
1,2,3,4,7,8-HxCDF	9.4	5.5-16	5.3	2.1-8.4	0.2
1,2,3,6,7,8-HxCDF	8.2	4.4-13	4.6	2.0-8.0	0.3
2,3,4,6,7,8-HxCDF	2.6	1.5-4.1	1.9	0.7-3.1	0.3
1,2,3,7,8,9-HxCDF	0.16	<0.3-<0.4	0.15	<0.3-<0.3	1.0
1,2,3,4,6,7,8-HpCDF	12	7.4-19	7.5	2.2-9.9	0.2
1,2,3,4,7,8,9-HpCDF	0.21	<0.3-<0.5	0.21	<0.3-<0.5	1.0
OCDF	2.5	<1-9.8	2.8	<2-10	0.1
Non-*ortho*-PCBs					
#77	7.2	4.8-13	5.0	3.8-5.9	0.2
#126	240	110-380	120	34-280	0.2
#169	160	120-200	110	53-170	0.1
TCDD Equivalents¤					
- excluding PCBs	56	30-94	21	8.2-34	0.02
- including PCBs	81	48-130	34	12-64	0.03

&Values below the detection limit were set at half that concentration.

* Wilcoxon's rank sum test for unpaired samples (two-tail).

¤ Refers to TCDD Toxic Equivalents: for dioxins and dibenzofurans, according to I-TEF for the non-ortho-PCBs, according to (11).