Effects of PCDD/F-exposure on thyroid- and thyroid-stimulating hormones in children and teachers exposed to wood preservatives in West-Germany

Karmaus W., Pless T.
NORDIG Institute for Health Research and Prevention, Norderstedt, FRG.

Introduction

In animal studies of acute and long term intoxication with high doses of 2,3,7,8-tetrachloro-dibenzo-p-dioxins (TCDD) and related compounds via food many symptoms resemble in several aspects the effects of hyperthyroidism, while in other aspects the toxic responses are characteristic of hypothyroidism. A structural activity relationship exists between TCDD and thyroxine. Investigations into the relationship between TCDD and tetraiodothyronine (thyroxine) and triiodothyronine in animals gave contradictory results: in some species a decrease of thyroxine and an increase of triiodothyronine and vice versa in other species.

Three epidemiologic studies analysed serum levels of thyroxine and thyroid-stimulating hormone (TSH) in humans exposed to polychlorinated dibenzo-dioxins and -furans (PCDD/F). Regarding thyroxine, one study showed a significant increase [1], two other investigations [2, 3] could not identify significant difference between exposed and non-exposed. Regarding TSH, two studies [1, 3] found a statistically significant increase in the exposed group.

The purpose of the study is to analyse if low-dose inhalative exposure to PCDD/F has an effect on the levels of triiodothyronine, thyroxine and TSH. This investigation was part of a project which was initiated in order to analyse a broader spectrum of possible health effects due to an exposure to wood preservatives in day care centers. The problem of an exposure to wood-preservatives in day-care centers containing PCDD/F, pentachlorophenol (PCP) and hexachlorocyclohexan (HCH) originated after several months of complaints which were originally attributed to formaldehyde.

Methods

The collection of the data is cross-sectional. However, since the population was exposed in different periods of their life and since the exposure ended in various time-periods before the investigation started, the study includes some elements of a longitudinal design.

The population consists of two groups which were investigated separately: Children: 420 exposed children and a comparison group of 205 unexposed, 211 exposed teachers and 189 references. The populations were recruited differently: The parents of exposed children were informed by the respective day-care center or the press. Parents of reference children were contacted in various ways: by exposed parents, by the press, by the investigators. Teachers: The exposed teachers were informed by their employers and by the trade unions. Teachers not exposed to wood preservatives in their day-care center were approached by the investigators in different day-care centers which were localized close to the exposed institutions.

All day-care centers in the state of Hamburg and its neighboring districts were checked for indoor panels that were treated with wood preservatives by local health authorities. In all day-care centers with a relevant amount of panels treated with wood-preservatives indoor concentrations of PCCD/F, PCP and HCH were measured [4]. Day-care centers with an indoor concentration of more the 0.5 pg TCDD-Equivalents (according to Toxic Equivalent Factor of the Federal Environment Office in the FRG: TEQ-FRG) per cubic meter were closed.

The information about the day-care centers which the child visited in the past or presently were gathered by telephone interviews with the parents. The data from the teachers were ascertained in personal interviews. According to this information, indoor levels of the substances were provided for each child and each teacher, including those in the reference group with past experience of exposure. It is assumed that the non-exposed population has an indoor exposure of zero. In order the take the reduction of exposure for a varying lengths of post-exposure periods into account, a "decay" of exposure with a half-life of 6 years after the ending of exposure was estimated per person.

Information about medical risk factors was gathered for the children or adults in a medical check-up The medical examination included the collection of blood samples. The samples were analyzed in the same clinical laboratory of the University Hospital Eppendorf with ELIZA (triiodothyronine, thyroxine: Enzymon-Kit, Boehringer; TSH: Amerlite-Kit, Amersham).

We analysed the data with linear regressions. Starting with an extensive set of potential confounders we reduced the model to the minimal set of confounders which was necessary for control but leaving those which would change the parameter estimate.

Results

Table 1: Frequency of children and teachers exposed to different concentrations of PCDD/F (TEQ-FRG) in indoor air of their day-care center

TCDD-Equivalents* (sum of particles and & gas;pg/m^3; grouped)	CHILDREN n	%	TEACHERS n	%
0	206	33.0 %	189	46.1 %
0 - 0.4	97	15.8 %	94	22.9 %
0.41 - 0.8	138	22.1 %	70	17.0 %
0.81 - 1.2	103	16.4 %	46	11.2 %
1.21 - 1.6	119	13.0 %	9	1.9 %
> 1.6	0		2	0.5 %
Total	625		410	

* Including a "decay" in the post-exposure period with a half-life of 6 years.

The indoor concentrations in exposed day-care centers ranges from 0.2 to 2.46 pg/m^3 TEQ-FRG. More children than teachers were exposed to concentrations above 0.8 pg/m^3 TEQ-FRG (table 1). In children there is nearly an equal distribution between male and females. On the other hand, teachers in day-care centers are mainly women. The frequency of the use of oral contraceptives, which is a 'risk-factor' of its own right for thyroxine and TSH, is not different in the exposed and unexposed group (table 2). The children are between 3 and 21 years of age, indicating first, a number of "children" who went to the day-care center after daily school hours, and second a num

ber of "children" who were exposed in previous years (table 2). The length of the post-exposure period is in the majority of both populations more than nine months. Thus only in a few cases the medical examination took place when the population still was in one of the exposed day-care centers.

Table 2: Frequency of some potential confounders

Some potential confounders		CHILDREN ex-posed (n=205)	CHILDREN non-ex posed (n=420)	TEACHERS ex-posed (n=211)	TEACHERS non-ex-posed (n=189)
GENDER	females	46.7 %	45.9 %	96.8 %	97.4 %
AGE	3 - 6 years	23.8 %	39.0 %		
	> 6 - 9 years	30.0 %	30.2 %		
	> 9 - 12 years	21.2 %	21.0 %		
	> 12 - 20 years	24.5 %	9.8 %	1.4 %	0
	> 20 - 30 years	0.5 %	0	28.9 %	35.4 %
	> 30 - 40 years			28.1 %	37.4 %
	> 40 - 50 years			26.7 %	18.0 %
	50 years & older			14.9 %	8.5 %
USE OF ORAL CONTRACEPTIVES		1.0 %	0	35.7 %	37.6 %
LENGTH OF THE POST-EXPOSURE PERIOD	up to 3 months	5.2 %	/	14.9 %	/
	> 3 to 6 months	4.3 %	/	34.8 %	/
	> 6 to 9 months	3.1 %	/	2.3 %	/
	more than 9 months	87.4 %	/	48.0 %	/

The comparison of means and medians in tables 3 and 4 only reveal a difference for TSH in children and in teachers. Controlling for confounders, these differences gained statistical significances ($p=0.0001$ and $p=0.046$ respectively). Regarding thyroxine and controlling for confounders, a significant effect of indoor exposure to TEQ-FRG in children showed up for the combined effect of intensity (concentration) and duration of exposure ($p=0.049$): Only children exposed for four years and more had an increase of thyroxine. In teachers the effect of the indoor concentration of TEQ-FRG was not significant ($p=0.096$), however, it showed a similar trend with increasing indoor concentrations. Regarding the analysis of triiodothyronine, there was no significant association with exposure in children. For teachers a non-significant ($p=0.06$) increase could be identified.

Discussion

The results show minor, however, significant effects of PCDD/F on the levels of thyroxine and thyroid-stimulation hormone (TSH) in the blood of two human populations which were investigated independently. The effects on TSH confirm the findings in animal studies. In humans, the effect on thyroxine seems to differ from the findings in animals.

These changes are no indicators of diseases. In the framework of prevention of toxic hazards, however, we have to consider early indication of health risks. Thus, these findings indicate that the inhalative route of exposures to low levels of PCDD/F should be considered more carefully in the future.

Table 3: Distribution of triiodo-thyronine, thyroxine and thyroidstimulating hormone

Variables of interest		Frequency % expos. group n=415	Frequency % unexp. group n=202	TEACHERS mean, std, percentiles exposed group		TEACHERS mean, std, percentiles unexposed gr.		Frequency % expos. group n=211	Frequency % unexp. group n=189	CHILDREN mean, std, percentiles exposed group		CHILDREN mean, std, percentiles unexposed gr.	
Tri-	≤ 1.00	1.2	0.5		1.51		1.54	10.9	10.1		1.29		1.27
iodo-	1.01-1.20	6.2	5.9		(0.24)		(0.22)	27.6	33.3		(0.28)		(0.24)
thyro-	1.21-1.40	23.9	18.4					31.6	31.2				
nine	1.41-1.60	38.1	37.6	50%:	1.5	50%:	1.52	19.5	16.4	50%:	1.26	50%:	1.23
in	1.61-1.80	17.6	25.2	5%:	1.15	5%:	1.19	13.2	6.4	5%:	0.94	5%:	0.93
µg/l	1.81-2.00	9.6	10.4	95%:	1.91	95%:	1.92	1.8	2.1	95%:	1.72	95%:	1.7
	2.01-2.20	1.7	1.5					1.3	0				
	> 2.20	0.7	0.5					0.5	0.5				
		n=414	n=201		n=414		n=201	n=221	n=189		n=221		n=189
Tetra-	≤ 70	8.2	9.0		87.11		89.35	14.0	16.9		86.41		85.5
iodo-	71- 80	25.1	19.4		(13.85)		(14.46)	22.2	22.8		(15.2)		(17.39)
thyro-	81- 90	30.2	27.3					27.1	23.8				
nine	91-100	23.5	24.4	50%:	86.0	50%:	89.0	19.1	19.0	50%:	86.0	50%:	84.0
in	101-110	7.7	10.9	5%:	66.0	5%:	67.0	10.4	10.1	5%:	64.0	5%:	59.0
µg/l	111-120	3.6	7.5	95%:	111.0	95%:	115.9	5.8	3.7	95%:	113.0	95%:	116.0
	> 120	1.7	1.5					1.4	3.7				
		n=404	n=198		n=404		n=198	n=221	n=189		n=221		n=189
Thyroid-	0.3-0.8	6.7	9.6		1.92		1.63	42.1	46.0		1.05		0.91
stimu-	0.9-1.4	27.5	40.4		(0.96)		(0.77)	36.2	42.9		(0.73)		(0.48)
lating	1.5-2.0	29.2	28.8					17.2	7.9				
hormone	2.1-2.6	19.0	12.1	50%:	1.7	50%:	1.5	2.7	2.7	50%:	0.9	50%:	0.9
(TSH)	2.7-3.2	8.7	5.6	5%:	0.8	5%:	0.7	0	0.5	5%:	0.2	5%:	0.2
in	3.3-3.8	4.7	1.0	95%:	3.7	95%:	3.0	0.5	0	95%:	2.0	95%:	1.8
mU/l	3.9-4.4	2.0	1.0					0.5	0				
	4.5-7.1	2.2	1.5					1.0	0				

Literature

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