CONTRIBUTION OF DIFFERENT PATHWAYS TO HUMAN EXPOSURE TO PCDDs/ PCDFs

Fürst, P.

Chemisches Landesuntersuchungsamt NRW
Sperlichstr. 19, 48151 Münster, Germany

Summary

Polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) are formed as unwanted by-products in a variety of industrial and thermal processes. These two classes of lipophilic and persistent contaminants are present in the environment since a very long time. They were not only identified in historical soil and herbage samples collected in England during the period from 1840 up to now[1] but were even determined in soil samples from a Roman brickworks on the Lower Rhine (Dormagen) dating back to between 70 and 40 B.C.[2] This demonstrates that PCDDs and PCDFs were already formed to a certain extent in much earlier times. However, their levels in the environment increased significantly with the beginning of industrial chlorine chemistry in this century. Due to the manifold sources PCDDs and PCDFs are meanwhile found in an ubiquitious distribution.

Humans may become contaminated with PCDDs/PCDFs through either

- occupational exposure,
- accidental exposure or
- environmental (background) exposure.

Investigations of workers occupationally exposed to chlorophenoxy herbicides or chlorinated phenols revealed in some cases several thousand ppt of 2,3,7,8-T_4CDD and other PCDD/ PCDF congeners characteristic for the respective production process. However, the highest body burden so far was found in blood from a child after the severe accident in a chemical plant in Seveso in 1976. In this sample a 2,3,7,8-T_4CDD level of 56000 pg/g blood fat was determined.[3] In contrast, human exposure caused by background contamination through secondary sources is several orders of magnitude lower. Blood samples of persons with no known exposure from

Germany analyzed in 1991/1992 showed 2,3,7,8-T_4CDD levels < 10 pg/g blood fat. Total PCDD/PCDF levels ranged between 10 and 110 pg I-TEq (NATO/CCMS)/g blood fat with a mean value of approximately 40 pg I-TEq (NATO/CCMS)/g blood fat.[4] This burden is caused by an average daily intake of 1-3 pg I-TEq (NATO/CCMS)/kg body weight.[5,6,8] While the situation in other industrialized countries seems to be very similar, human samples from developing countries normally show lower PCDD/PCDF levels indicating a lower exposure for the normal population. This was inter alia demonstrated by a field study conducted by WHO/EURO where breast milk samples were analyzed from various countries world-wide.[7] All investigations performed so far indicate that exposure to PCDDs/PCDFs for the normal population increases with the degree of industrialization of the respective country where the people live.

Meanwhile it is generally agreed upon that for the normal population diet represents the main route of exposure to PCDDs/PCDFs. Usually more than 90% of the total daily intake of these contaminants derives from food. In contrast, exposure via other routes normally contributes to less than 10%. Because humans stand at the top of the food chain it becomes obvious that human tissue may contain relative high amounts of those xenobiotics such as PCDDs/PCDFs which tend to bioaccumulate within the food chain. This is of special importance for breast milk which represents the first food-stuff for the newborn baby. Taking the data of the above mentioned WHO/EURO study into account and assuming an intake of 800 ml milk with 3% fat this would result in an average daily intake of 94 pg I-TEq (NATO/CCMS)/kg body weight for a baby weighing 5 kg. Although the tolerable daily intake (TDI) concept which is based on a life time intake should not be applied to the relative short nursing period the estimation of the daily PCDD/PCDF intake for babies via breast milk exceeds all proposed TDI values ranging from 0.006-10 pg/kg body weight/day. Investigations of the past four years in Germany revealed a decline of PCDD/PCDF levels in breast milk.[17] This might be an indication that the efforts undertaken to minimize dioxin emissions and to shut down known sources have already had a beneficial effect on the body burden of humans.

Occupational/Accidental Exposure

In the past few years a lot of extensive surveys were performed in order to assess the body burden of humans who have been occupationally or accidentally exposed to PCDDs/PCDFs. In most cases these investigations did also comprise follow-up or epidemiological studies on the long term hazards associated particularly with 2,3,7,8-T_4CDD. For example, the retrospective cohort study of mortality conducted by NIOSH

included 5172 workers at 12 plants in the United States that produced chemicals, such as chlorinated phenols, chlorophenoxy herbicides, insecticides and bactericides all contaminated with 2,3,7,8-T_4CDD.[8] Occupational exposure was not only documented by reviewing job descriptions but also by measuring 2,3,7,8-T_4CDD in serum of 253 workers. The highest level in this cohort was found to be 3400 pg 2,3,7,8-T_4CDD/g blood fat. In a recent investigation 2,3,7,8-T_4CDD levels up to 291 pg/g fat were determined 22 years after exposure in adipose tissue of workers from a Russian herbicide plant which produced 2,4,5-T.[9]

While high levels of 2,3,7,8-T_4CDD are characteristic of occupational exposure from production of trichlorophenol containing products, different marker congeners are found in human specimens after occupational exposure from other processes such as production of pentachlorophenol (PCP). In blood samples collected from workers in a PCP plant OCDD levels ranged up to 285000 pg/g blood fat. The maximum H_7CDD level in this cohort was 22500 pg/g blood fat.[10] In 1986 an investigation of Boehringer workers occupationally exposed in the 1950s during the production of lindane, chlorinated phenols and 2,4,5-T revealed levels up to 2250 pg 2,3,7,8-T_4CDD, 605 pg P_5CDD, 9600 pg H_6CDDs, 4100 pg H_7CDD and 16000 pg OCDD/g adipose tissue, based on fat weight.[11]

The most severe accident known so far happened in Seveso in 1976 when a reaction vessel went out of control with the consequence that several hundred grams of 2,3,7,8-T_4CDD were released into the environment. The resulting exposure for inhabitants especially living in the highest contaminated A-zone was enormous. The highest 2,3,7,8-T_4CDD level in this cohort was found to be 56000 pg/g blood fat.[3]

Other reported events with severe health effects caused by accidental exposure, however with different contamination patterns, involve consumption of pentachlorophenol containing olive oil in Spain[12] as well as ingestion of contaminated rice oil in Yusho and Yucheng. The latter exposure will be discussed along with the results of the follow-up studies in detail in other papers of this issue.

Exposure through background contamination

While specimens from humans who have been occupationally or accidentally exposed normally are dominated by the PCDD/PCDF congeners which are characteristic of the respective source or process, samples of humans being exposed through background contamination show a more unique congener pattern.

Human exposure through background contamination is possible by several routes:

- inhalation of air and ingestion of particles from air
- ingestion of contaminated soil
- dermal absorption and
- food consumption

The share of each route to the daily intake differs considerably due to the physico-chemical properties of PCDDs/ PCDFs. An estimation of human intake can be performed either by application of pharmacokinetic models or preferably by calculation using analytical data for the matrices in question. In any case this assessment can only result in a rough estimation reflecting an average intake of the normal population. Using the latest research data on environmental levels a WHO expert group performed in 1990 an assessment of human PCDD/PCDF intake by using a pathway analysis taking into account all known important routes of exposure.[13] It has to be stated that this kind of estimation deals only with the intake which is presumably higher than the actual body uptake due to different absorption rates for the various exposure routes.

The following table shows the results of this pathway analysis. It simultaneously demonstrates the relative significance of the various exposure routes.

source	pg I-TEq/day	pg I-TEq/kg body weight/day
food	70 - 200	1 - 3
air	4	0.06
soil	0.5 - 5	<0.01 - 0.07

An additional daily PCDD/PCDF intake may be derived from miscellaneous potential sources.[14]

source	pg I-TEq/day	pg I-TEq/kg body weight/day
cigarettes	1.6 - 3	0.02 - 0.04
coffee filter*	8.2	0.1
milk cartons*	29	<0.01 - 0.07

* Levels marked by an asterisk are based on data from 1988. Actual levels are distinctly lower.

In summary, all routes of exposure through background contamination lead to an average daily intake of 1-3 pg I-TEq (NATO/CCMS)/kg body weight. Usually more than 90% of this intake derives from food. Due to the lipophilic nature of PCDDs/

PCDFs, food-stuffs of animal origin are of special importance. Normally dairy products, meat and meat products, and fish and fish products each contribute approximately 30% of the daily PCDD/PCDF intake via food. However, this share may differ to a certain extent due to various consumption habits or if food-stuffs from contaminated areas are consumed. This is especially true for people with high consumption of fish from the Baltic Proper. Blood analyses of those people showed elevated PCDD/PCDF levels.[15] Increased PCDD/PCDF levels were also found in blood samples from residents living in a contaminated area in Rheinfelden/Germany. Yearly consumption of approximately 300 eggs from foraging chickens kept in this area with levels up to 300 pg I-TEq (NATO/CCMS)/g egg fat resulted in a human blood level of 156 pg I-TEq (NATO/CCMS)/g fat.[16]

In any case, even a daily intake of 1-3 pg I-TEq (NATO/CCMS)/kg body weight estimated as a normal background exposure already exceeds the tolerable daily intake set by health authorities in several countries. This demonstrates the need to reduce the emissions of PCDDs and PCDFs to levels as low as technically achievable in order to minimize the ubiquitious contamination of the environment and thus finally to achieve a reduction of the body burden in humans.

Exposure of breast fed babies to PCDDs/PCDFs

Measures to minimize emissions are especially mandatory to reduce PCDD/PCDF levels in breast milk because of its importance as the first food for the newborn child. Due to the public concern about contaminants in breast milk, some health authorities and governments, especially in Germany, offer nursing mothers an analysis of their breast milk for PCDDs/PCDFs. Within these surveys more than 1500 individual breast milk samples have meanwhile been analyzed in Germany since 1984.

Since breast milk represents a good substrate to examine the background contamination, WHO/EURO conducted a world-wide field study on contamination of breast milk with PCDDs/PCDFs.[7] The results showed that PCDD/PCDF patterns as well as levels in breast milk from various industrialized countries were very similar. An interesting exeption is, however, that breast milk samples from the United States contain significantly lower levels of 2,3,4,7,8-P_5CDF than specimens from Western Europe indicating a somewhat different source of exposure.[18] The reason for this finding is still unknown. Calculated as toxic equivalents, the PCDD/PCDF levels analyzed within the WHO field study ranged from 8.2-40.2 with a mean value of 22.4 pg I-TEq/g fat. Breast milk samples from developing countries actually show a

comparable pattern, however the levels were found to be lower compared to those specimens from industrialized countries. Thus, to a certain extent PCDD/PCDF levels in breast milk seem to reflect the degree of industrialization of the country where the mother lives.

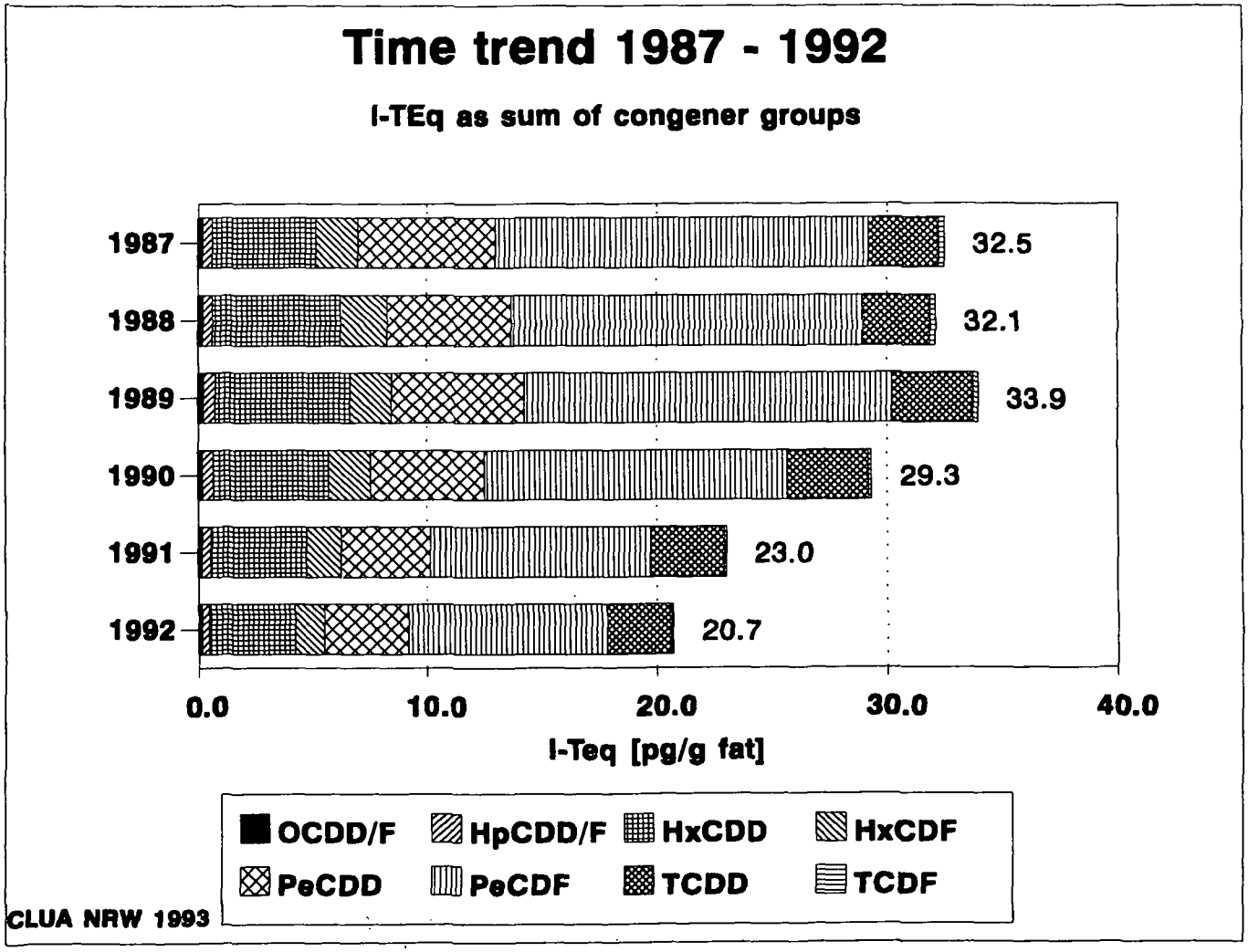
Based on the analytical data from the WHO study and assuming a daily consumption of 800 ml milk with 3% fat, this would result in an average daily intake of 94 pg I-TEq/ kg body weight for a baby weighing 5 kg. Consequently, the average daily PCDD/ PCDF intake for a breast fed baby is approximately 50 times higher than the average daily PCDD/PCDF intake for an adult.

The most important factors which influence the dioxin levels in breast milk are the number of breast fed children, the total length of nursing periods and the age of the mother. While the levels decrease with increasing number of breast fed children and the length of the nursing period, they increase with the age of the primigravida. On the other hand, the area of domicile, whether urban or rural, seems to have no effect on the body burden with these contaminants.

Figure 1 depicts PCDD/ PCDF levels in breast milk over the course of the years 1987-1992.[17] The bars represent the mean I-TEq levels as sum of congener groups for each year. It becomes clear that the analyses of the past three years show a tendency to lower levels. This decline is mainly due to lower levels of 2,3,4,7,8-P_5CDF, H_6CDDs and 2,3,7,8-T_4CDF, whereas 2,3,7,8-T_4CDD remains almost constant. Comparable time trends were reported for breast milk samples from Lower Saxony/ Germany[19] and for blood samples collected from persons with no known exposure in Germany.[20] These results seem to indicate that efforts to reduce emissions such as the following measures are already beginning to have effects to a certain extent:

- optimization of incineration technology
- ban of production and use of PCP in several countries
- phasing out of leaded gasoline with halogenated scavengers
- substitution of chlorine in paper pulp bleaching with other reagents

Although no adverse health effects in a baby have been causally linked so far with background tissue concentrations of PCDDs/PCDFs and despite the declining trend of the levels, the exposure of babies during the breast feeding period must still be considered as a matter of concern and justifies the measures to be taken to reduce PCDD/PCDF emissions into the environment.


Time trend 1987 - 1992
I-TEq as sum of congener groups
1987
1988
1989
1990
1991
1992
32.5
32.1
33.9
29.3
23.0
20.7
0.0
10.0
20.0
30.0
40.0
I-Teq [pg/g fat]
OCDD/F
HpCDD/F
HxCDD
HxCDF
PeCDD
PeCDF
TCDD
TCDF
CLUA NRW 1993

References

1 Kjeller LO, Jones KC, Johnston AE, Rappe C. *Environ Sci Technol* 1991;25:1619-27.
2 Hartmann P, Grupe A, Neupert M. *UWSF-Z Umweltchem Ökotox* 1992;4:197.
3 Mocarelli P, Patterson DG, Marocchi A, Needham LL. *Chemosphere* 1990;20:967-74.
4 Schrey P, Wittsiepe J, Ewers U, Exner M, Selenka F. In: *Organohalogen Compounds Vol.9,* Finnish Institute of Occupational Health. Helsinki 1992:261-67.
5 Beck H, Eckart K, Mathar W, Witkowski R. *Chemosphere* 1989;18:417-24.
6 Fürst P, Fürst Chr, Groebel W. *Chemosphere* 1990;20:787-92
7 WHO/EURO. Environmental Health Series Vol. 34. FADL Publisher. Copenhagen 1989.
8 Fingerhut MA, Halperin WE, Marlow DA et al. *N Engl J Med* 1991;324:212-28
9 Schecter A, Ryan JJ, Päpke O, Ball M. In: *Organohalogen Compounds Vol.9,* Finnish Institute of Occupational Health. Helsinki 1992:247-50.
10 Päpke O, Ball M, Lis A. *Chemosphere* 1992;25:1101-08
11 Beck H, Eckart K, Mathar W, Witkowski R. *Chemosphere* 1989;18:507-16.
12 Rodriguez-Ricardo A, Camacho F, Rappe C, Hansson M, Smith AG, Greig JB. In: *Organohalogen Compounds Vol.1.* Eco-Informa Press. Bayreuth 1990:297-300
13 Fürst P, Beck H, Theelen R. *Toxic Substances Journal,* in press.
14 Beck H, Droß A, Mathar W. *Chemosphere* 1992;25:1539-50
15 Svensson G, Nilsson A, Hansson M, Rappe C, Akesson B, Skerfving S. In: *Organohalogen Compounds Vol.1.* Eco-Informa Press. Bayreuth 1990:505-08.
16 Wuthe J. In: *Current views of the impact of dioxins and furans on human health and the environment,* Berlin Nov.9-11 1992. The Toxicology Forum 1993:252-63.
17 Fürst P, Fürst Chr, Wilmers K. *Chemosphere* 1992;25:1029-38.
18 Schecter A, Fürst P, Krüger Chr, Meemken HA, Groebel W, Constable JD. *Chemosphere* 1989;19:979-84.
19 Ende M, Personal communication 1993
20 Päpke O, Ball M, Lis A. This issue