Age Dependent Levels of PCDD and PCDF in Human Blood Samples

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ABSTRACT

Combining PCDD/PCDF levels in 69 blood samples from various studies in northern Germany, it can be shown that PCDD/PCDF accumulate with age, and that the relation between body load and age follows a straight line with an increment of about 0.6 ppt ITE per year. To distinguish between normal body burdens and high body burdens requiring further investigation, it seemes inadequate to use one single value as a criterion. Instead, the use of a function is proposed which is derived from the 95 % upper limit of the prediction interval. Within the range of 5 up to 85 years of age, elevated PCDD/PCDF-levels in blood (in ppt ITE) would be defined as being in excess of 0.6 times age (in years) plus 28.

OBJECTIVES

Due to their long elimination half-lives, polychlorinated dibenzodioxins and dibenzofurans (PCDD/PCDF) tend to accumulate in human tissues. Therefore, an age dependence of PCDD/PCDF concentrations in human tissues has been suggested[1]. BECK was the first to show this relationship from his studies on PCDD/PCDF concentrations in human fat tissue and breast milk[2]. However, his data were too sparse to allow for a regression of PCDD/ PCDF levels on age. In this paper, we report on PCDD/PCDF concentrations determined in blood samples from 36 children and 33 adults living in northern Germany. These data were pooled and used to assess the age dependence of PCDD/PCDF levels and to propose an age dependent criterion distinguishing between normal and elevated concentrations.

MATERIAL AND METHODS

Data were obtained from studies conducted in 4 places in northern Germany. Potential exposures to toxic metals and PCDD/PCDF by ingestion and/or inhalation had prompted these investigations. The composition of the studied populations is as follows:

- 12 children aged 9 to 13 from an urban residential area with contaminated soil (<4 ppb) source: contaminated land fill
- 9 children aged 8 to 13 from a rural residential area with contaminated soil (<8 ppb) source: mixture of slag and fly ash from a municipal waste incinerator covering a car park
- 15 children aged 7 to 17 from an urban residential area serving as controls
- 14 adults aged 25 to 65 from an urban residential area with contaminated soil (<0.8 ppb) sources: former cable burner, active lead smelter, indoor air (PCP-treated wood)
- 14 adults aged 33 to 64 from an urban residential area with contaminated soil (<4 ppb) source: contaminated land fill
- 5 adults aged 26 to 51 working on a toxic waste dumpsite containing tons of PCDD/PCDF.

PCDD/PCDF concentrations in blood samples were determined by the Institute of Hygiene of the Ruhr Area, Gelsenkirchen, and by the ERGO company, Hamburg. The latter successfully participated in the the WHO interlaboratory dioxin-in-blood study. Except for controls which were drawn at random, the selection of the study participants was restricted to persons with heavy exposures. As no relevant differences were observed between the blood levels of exposed persons and controls, the data were combined into one single data set, from which age dependent mean PCDD/PCDF levels in blood were calculated by linear regression. In search of a useful criterion to distinguish between normal and elevated PCDD/PCDF levels, the 95 % upper limit of the prediction interval[3] was selected; it is also referred to as tolerance limit in the literature[4]. Profiting from the fact that the graph of this function is practically linear and in parallel of the least squares fit, it was approximated by a straigt line having the same increment as the linear regression line. This makes calculations much easier; however, the precise 95 % upper prediction limits are shown in the graphs (figs. 1,2) along with the formulae describing the corresponding surrogate functions.

RESULTS

The concentration of PCDD/PCDF in blood samples obtained from 36 children and 33 adults are shown in fig. 1. Additional data obtained from 56 adult controls living in a rural area in Northrhine-Westfalia (Steinfurt county) have been added to the graphs for comparison. Since from the Steinfurt data only the median values of the age and body burden distributions have been published so far[5], they could not enter into the data pool underlying this study. However, it is obvious from the graphs (figs. 1,2), that these controls do not have lower PCDD/PCDF blood levels than the populations making up for most of the data used in this meta-analysis. Also for comparison, PCDD/PCDF levels in body fat of 6 infants who died from Sudden Infant Death Syndrome (SIDS) are shown in the graphs (figs. 1,2)[6]. Even though they would fit quite well to the rest of the data, they were not considered because it is not clear whether or not the toxicodynamics of PCDD/PCDF uptake and accumulation in infants is comparable to that of children and adults. In a separate step, PCDD/PCDF levels in fat tissue of deceded persons were taken from the literature[1,2] and added to the data pool. Inclusion of these data leads to a steeper increment of the least squares fit, and to a considerable gain in variance (fig. 2). Therefore, the age dependent mean and the age dependent 95 % upper prediction limits are given separately:

PCDD/PCDF in blood, least squares fit: $y = 0.6\,x + 10$
PCDD/PCDF in blood, 95 % upper prediction limit: $y = 0.6\,x + 28$

PCDD/PCDF in blood or fat, least squares fit: $y = 0.8\,x + 7$
PCDD/PCDF in blood or fat, 95 % upper prediction limit: $y = 0.8\,x + 38$

(y = PCDD/PCDF level in ppt ITE; x = age in years)

DISCUSSION

The results of this study confirm the age dependence of PCDD/PCDF concentrations in human tissues as first shown by BECK[2] on a qualitative level. Thanks to the availability of more data on children and young adults, we were now able to assess the age dependence of PCDD/ PCDF concentrations quantitatively. Furthermore, the 95 % upper prediction limit could be calculated as a measure of variance of the data; it lends itself to make a distinction between normal values and elevated values deserving further investigations into the reasons for such extraordinary exposures.

From his data, BECK had proposed an upper margin of the background body burden of about 140 ppt ITE[7]. Not being able to account for the age dependence of PCDD/PCDF levels, it is obvious that his reference value is too high, especially for young adults and children. Another reason for the discrepancy between his criterion and the one proposed by us is that his was based on results of PCDD/PCDF determinations in fat tissue going back to 1986/1987. As shown here (fig.1 vs fig.2), these early determinations not only indicate a higher body load, but also exhibit a larger variance. This difference is mostly due to the greater dispersion of PCDD/PCDF levels in elderly persons. One has to take into account that weight loss before death can fake high fat levels never experienced during lifetime. Since it could be demonstrated that blood levels and fat tissue levels correspond with eachother very well[8], the data presented here could also suggest a slight decrease in human body burden over the last years. As the data base on PCDD/PCDF levels in human blood samples will improve, adaptive changes to the model proposed above to describe the upper limit of "normal" levels may be necessary in the future.

REFERENCES

1 Thoma H, Mücke W, Kretschmer E. Untersuchung von Humanfettproben auf PCDD/PCDF. *VDI-Berichte* 1987;634:383-387.

2 Beck H, Droß A, Mathar W. Polychlorierte Dibenzodioxine und dibenzofurane in Lebensmittel- und Humanproben einschließlich Frauenmilch. *BMFT-Abschlußbericht, Förderkennzeichen 0765001*. 1991.

3 Sachs L. *Angewandte Statistik*. Sechste Auflage. Springer Verlag Berlin, 1984.

4 *Geigy Scientific Tables*, Volume 2. 8th Edition. CIBA-GEIGY Basel, 1982.

5 Ministerium für Arbeit, Gesundheit und Soziales des Landes NRW. *Kieselrot-Studie, Humanmedizinische Untersuchungen.* Bericht des Hygiene-Instituts des Ruhrgebiets, 1991.

6 Beck H, Droß A, Kleemann W J, Mathar W. PCDD and PCDF concentrations in different organs from infants. *Chemosphere* 1990;20:903-910.

7 Beck H, Eckart K, Mathar W, Wittkowski R. Levels of PCDDs and PCDFs in adipose tissue of occupationally exposed workers. *Chemosphere* 1989;18:507-516.

8 Schecter A, Ryan J J, Päpke O, Ball M. Comparison of dioxin and dibenzofuran levels in whole blood, blood plasma and adipose tissue, on a lipid base. *Organohalogen Compounds* 1990;1:279-281.

Fig.1

Age Dependent Levels of Dioxins in Human Blood Samples
(fat samples not considered)

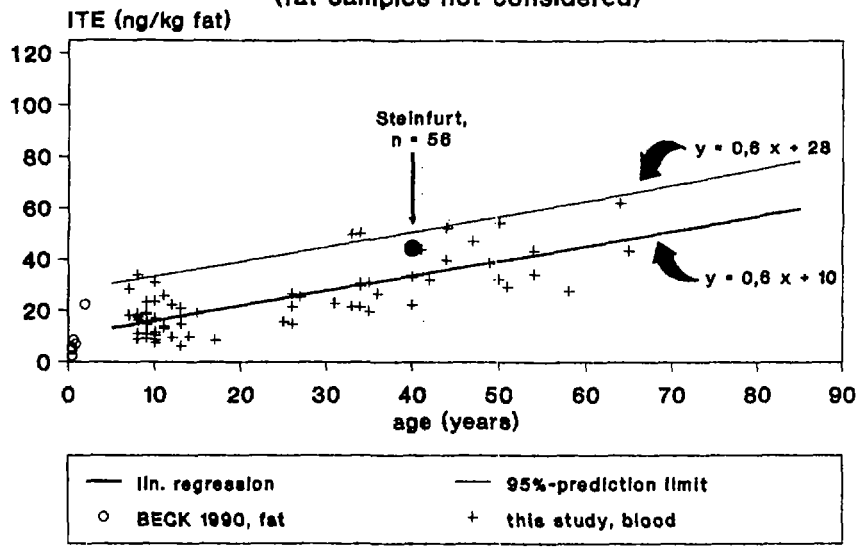

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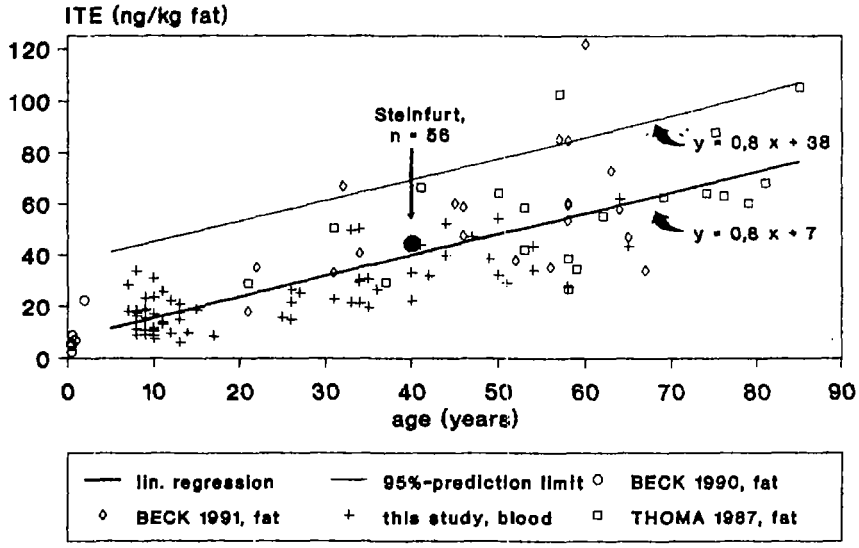
Fig.2

Age Dependent Levels of Dioxins in Human Blood and Fat



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