# BLOOD KINETICS IN TWO PATIENTS SEVERELY CONTAMINATED WITH 2,3,7,8-TETRACHLORODIBENZO-*P*-DIOXIN

Alexandra Geusau[1], Olaf Päpke[2] and Klaus Abraham[3]

[1]Department of Dermatology, Division of Immunology, Allergy and Infectious Diseases (DIAID), University of Vienna, Medical School, Währinger Gürtel 18-20, A - 1090 Vienna, Austria.
[2]ERGO Forschungsgesellschaft mbH, 22305 Hamburg, Geierstraße 1, Germany.
[3]Department of Pediatric Pneumology and Immunology, Children's Hospital, Charité, Humboldt University, Augustenburger Platz 1, 13353 Berlin, Germany.

## Introduction

In spring 1998, severe 2,3,7,8- tetrachlorodibenzo-*p*-dioxin (TCDD) intoxication was diagnosed in two women working in the same company. The appearance of chloracne led to the diagnosis in both patients, in one of them (patient 1) there was a dramatic progression of the disease observed within one year, whereas patient 2 suffered only from mild chloracne. Over a period of more than 3 years, TCDD blood levels were monitored in these two patients and the half-lives were evaluated under the various strategies carried out to enhance TCDD elimination.

## Subjects and Methods

As previously reported, both patients had completed a trial involving the consumption of potato-chips containing olestra, a non-digestible, non-absorbable dietary fat substitute[1]. Accordingly, the patients continued with the intake of olestra either as a pure substance or in potato-chips (Pringle's fat-free chips, 28 g containing 10 g olestra; provided by Procter & Gamble, Cincinnati, Ohio, USA), in convenient amounts. The total dose of olestra from August 1998 to October 2001 was 8.2 kg in patient 1 and 5.5 kg in patient 2. Each of the patients received vitamins A, D, E and K, whose blood levels were regularly checked.

In addition, in patient 1, lipoprotein (LDL)-apheresis, an extracorporal means of blood lipid elimination, was carried out for a period of eight months. The high TCDD levels in these patients also allowed the measurement of TCDD elimination via the feces, skin and urine. TCDD excretion via these pathways was compared and their contribution to the overall elimination was calculated. The TCDD blood levels were regularly monitored between spring 1998 to October 2001. Whole blood was collected before breakfast on 26 occasions in patient 1 and on 21 in patient 2 using heparinized vials, which were stored and frozen until analysis. TCDD analysis was carried according to protocols as previously reported[2,3].

## Results and Discussion

There was a decrease of the TCDD blood levels from the initially 144,000 pg/g in patient 1 to 26,800 pg/g blood fat and from 26,000 pg/g to 7,300 pg/g blood fat in patient 2, measured in a time period from spring 1998 to October 2001. The time course of TCDD in blood fat indicated overall half-lives of 590 days (1.6 years) and 980 days (2.7 years) for patient 1 and 2, respectively. The overall half-lives observed in our patients are considerably shorter than those reported in other studies[4,5,6,7]. During the observation period no major change of body weight possibly affecting the TCDD blood levels was observed.

With these two patients, whose initial TCDD blood levels exceeded levels ever reported for adults, we had the opportunity to get information about the TCDD blood kinetics in two severely intoxicated persons assuming first order kinetics in a one compartment model (body fat mass). The influence of various treatment strategies and of different elimination pathways was evaluated: elimination via urine is negligible, elimination via skin is also of minor relevance as it represents only 1-2 % of the overall elimination rate[8]. In contrast, fecal excretion of TCDD as the parent substance was about 3- to 5-times higher. As previously reported, it can significantly be enhanced by the intake of olestra[1]. The three year olestra consumption contributed to about 9 % (patient 1) and 12 % (patient 2) of the overall elimination. This contribution would have been significantly higher in case of typical half-lives of approximately 7 years reported for low and moderately exposed subjects. When performed twice a week, removal of blood lipids by LDL-aphereses was comparable to TCDD elimination via fecal fat. Under the observed half-lives, about 78 % (patient 1) and 68 % (patient 2) of the daily TCDD clearance remained unexplained. This part can be assumed to account for metabolism, most likely resulting from induction of hepatic metabolism. It can be hypothesized that the short TCDD half-lives in our patients are a dose-dependent phenomenon in case of very high exposure [9,10,11].

**References**

1. Geusau A, Tschachler E, Meixner M, Sandermann S, Päpke O, Wolf C, Valic E, Stingl G, McLachlan M (1999) Lancet 354:1266-1267
2. Päpke O (1989) Chemosphere 19: 941-948
3. Päpke O (1997) Organohalogen Compounds. 31: 212-214
4. Flesch-Janys D, Becher H, Gurn P, Jung D, Konietzko J, Manz A (1996) J Toxicol Environ Health. 47: 363-378
5. Michalek JE, Pirkle JL, Caudill SP, Tripathi RC, Patterson DG, Needham LL (1996) J Toxicol Environ Health. 147: 209-220
6. Michalek JE, Pirkle JL, Needham LL, Patterson DG, Caudill SP, Tripathi RC, Mocarelli P (2002) J Exposure Anal Environ Epidemiol. 12: 44-53
7. Needham LL, Gerthoux PM, Patterson DG, Brambilla P, Pirkle JL, Tramacere PL, Turner WE, Beretta C, Sampson EJ, Mocarelli P (1994) Organohalogen Compounds. 21: 81-85
8. Geusau A, Tschachler E, Meixner M, Päpke O, Stingl G, McLachlan M (2001) Br J Dermatol. 145: 938-943
9. Carrier G, Brunet RC, Brodeur J (1995) Toxicol Appl Pharmacol. 131: 253-266
10. Carrier G, Brunet RC, Brodeur J (1995) Toxicol Appl Pharmacol. 131: 267-276
11. Geusau A, Schmaldienst S, Derfler K, Päpke O, Abraham K. (2002) Arch Toxicol. *in press*