# BODY BURDENS OF ORGANOHALOGENS IN CALIFORNIA POPULATIONS

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## Introduction

Due to their lipophilic properties, organohalogen compounds bioaccumulate in the food chain, with diet accounting for over 90% of non-occupational exposures. Human milk, serum, and adipose tissues have been used successfully to monitor body burdens of lipophilic chemicals, and surveys of targeted populations with consistent protocols have enabled researchers to examine trends and to compare groups[1]. Downward trends in dioxin body burdens have been shown in Sweden[2], The Netherlands[3], and Germany[4], while upward trends in PBDEs were shown in Sweden[2]. No such trends can be established for the USA because there are no systematic monitoring programs. The National Human Adipose Tissue Survey (NHATS[5]), a systematic nation-wide study, included dioxin analyses only in 1982 and 1987, and has since been discontinued. The lack of data from California impedes the work of public health and regulatory agencies and fuels concerns from citizens. We are currently conducting studies that will generate such needed data. In this paper we present data on persistent halogenated contaminants in adipose tissues of women undergoing breast surgery. These women comprise the control group in a breast cancer case-control study centered in the San Francisco Bay Area, and the data are compared to similar measurements from a decade ago. In addition, we examine distributions of the target chemicals in breast and abdominal adipose of women undergoing mastectomies with breast reconstruction. If concentrations were equivalent, use of abdominal adipose would greatly enhance the pool for controls for future epidemiological studies.

## Experimental Methods

Study populations. Women undergoing breast surgery for suspected breast cancer at Stanford University were recruited in the study. Small amounts of breast adipose tissue were collected during surgery and women were interviewed regarding demographics, exposures, medical and reproductive histories. Only controls are included in the body burden comparison. To study the distribution of chemicals in breast and abdominal adipose, we focused on women undergoing mastectomies with simultaneous breast reconstruction using abdominal tissue. Most were cases, although one with benign disease and three with ductal carcinoma in situ were also included.

Sample Analysis. Samples were stored at -20 °C until analysis. Samples were thawed, weighed, mixed with $Na_2SO_4$, homogenized with 1:1 dichloromethane:hexane, and spiked with $^{13}C$-labeled internal standards (all seventeen 2,3,7,8-PCDD / PCDFs; PCBs #77, 126, 169, 28, 52, 47, 101, 105, 118, 153, 180, 194, 209; HCB, ,-HCH, DDE, DDT, Dieldrin, Mirex and PBDE 77). ∝pproximately *1/10* of the extract was analysed for OCPs, PCBs and PBDEs, and 9/10 analysed for PCDD/Fs and coplanar PCBs. Lipid content was determined gravimetrically. Samples were

serially processed through columns containing $Na_2SO_4$ and AX21 Carbon. The first fraction off the carbon column was further cleaned up by GPC and Florisil, recovery standards were added and the sample concentrated to 10 ÌL for PCB, OCP and PBDE analysis. PCDD/Fs and coplanar PCBs were eluted from the carbon column with toluene and the eluate cleaned up with alumina and acid silica columns; recovery standards were added and the sample concentrated to 10 ÌL.

PCDD/Fs and PCBs were analyzed by HRGC/HRMS (Finnigan MAT 90) with a 60m, 0.25 mm ID, 0.25 μm film thickness, DB-5ms column. PFK was used for the lock masses and the MS was operated in an EI mode with multiple ion monitoring. OCPs and PBDEs were analyzed by LRMS in ECNI mode (Finnigan 4510) with a 60m, 0.25 mm ID, 0.25 μm film thickness, DB5ms column, with methane as the reagent gas. The ion source pressure was 0.6 Torr and ion source temperature was 100 °C. The electron energy was typically 70eV and the electron current was kept at 0.3 mA.

**Results and Discussion**

All results were expressed on a lipid basis. Because of the small size of the adipose samples, and their often low lipid content, many congeners were below the detection limit (DL). For those congeners, half the DL was used to calculate TEQs. Nevertheless, congeners which were consistently non-detected (below DL in over 50% of the samples) were not used for statistical analysis. In addition, a new summary measure (Adjusted TEQ) was devised incorporating only those congeners that were consistently measured above the DL. The eight congeners that comprised the Adj-TEQ are shown in Table 1. The conventional I-TEQs correlated well with the Adj-TEQs ($R^2$=0.98, $p<0.0001$) and, therefore, Adj-TEQs were used in statistical analyses to minimize uncertainties. In addition, Adj-TEQs allowed comparison with other data sets where most congeners were reported above detection, mainly because larger sample weights had been analyzed. To facilitate comparisons across data sets, the I-TEQ[6] system was used on all data. When the WHO-TEQ[7] system was used, our TEQs increased by approximately 2-3 pg/g fat.

Major PCDD/PCDF congeners in adipose of cancer-free women are shown in Table 1 and Fig.1, along with measurements from a 1988 survey[8] of women undergoing surgery in area hospitals for reasons other than cancer. The pattern of the prevalent congeners is consistent across data sets and also consistent with congener patterns reported as the nationwide average estimated concentrations from the 1987 NHATS survey[5] (Fig 1). Statistically significant decreases were found in the levels of I-TEQ, Adj-TEQ and all but one major congeners from the 1988 to the 1998 data sets. As the age distributions of the SF-1998 and SF-1988 women were similar (p=0.89), the decrease is not confounded by age. This first documented decrease in California dioxin body burdens is consistent with worldwide observed decreases. PCB and OCP concentrations are shown in Table 2. Patterns and levels are, in general, similar to those reported from other industrialized regions.

There were strong and significant correlations among all PCDD/F congeners and TEQ (with both old[6] and new[7] TEFs). TEQs correlated significantly with most PCBs and with HCB and , -HCH, but not with other OCPs. Most OCPs correlated with each other, while DDE and trans-nonachlor also correlated with many PCB congeners. Age and lactation history were examined as predictors of body burdens. The data suggest surrogate markers of exposure that may optimize future studies.

Paired analyses of breast and abdominal tissues showed no bias and no statistically significant differences in concentrations. This finding allows future studies to use either abdominal or breast adipose tissue for measurements of lipophilic chemicals, greatly enhancing selection of subjects.

Figure 1. Major PCDD/PCDF congeners in adipose tissues from the SF Bay Area in 1998 and 1988, and from NHATS-87

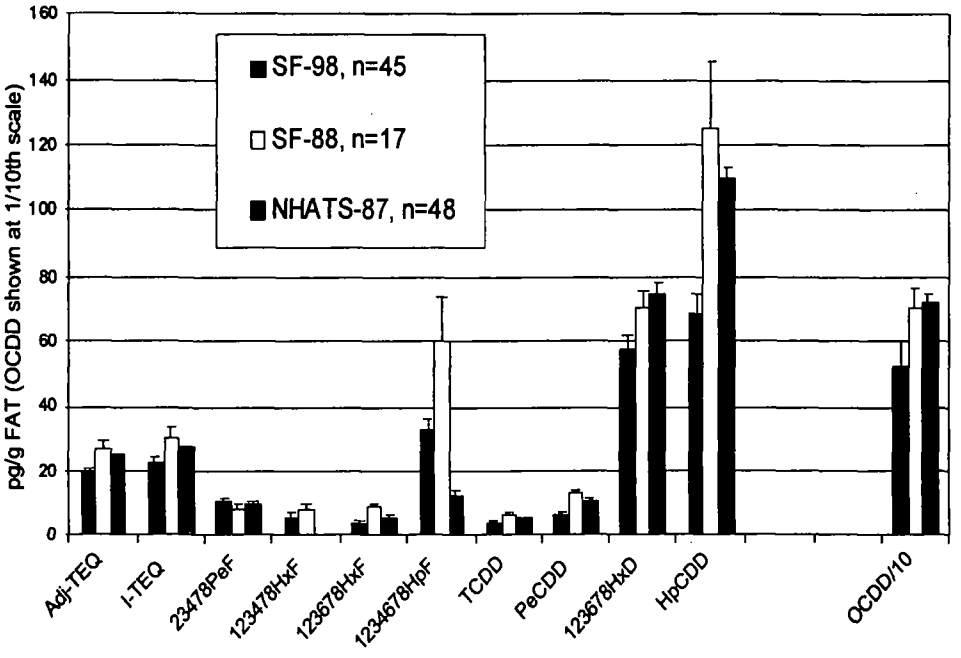


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**Table 1. Major PCDD/PCDF concentrations (pg/g fat) in breast adipose tissue (vs. 1988)**

| | SF-1998, n=45 | | | SF-1988, n=17 | | | |
|---|---|---|---|---|---|---|---|
| | % >DL | MEDIAN | RANGE | % >DL | MEDIAN | RANGE | p * |
| 2378-TCDD | 55 | 3 | 0.4-20 | 100 | 5.9 | 2.3-12.5 | 0.002 |
| 12378-PeCDD | 44 | 4 | 0.4-24 | 100 | 12.6 | 4.4-25 | 0.001 |
| 123678- HxCDD | 100 | 54 | 21-180 | 100 | 65 | 32-124 | 0.03 |
| 1234678- HpCDD | 100 | 60 | 23-200 | 100 | 108 | 34-334 | 0.003 |
| OCDD | 100 | 396 | 169-3230 | 100 | 760 | 137-1230 | 0.004 |
| 23478- PeCDF | 89 | 9 | 2-26 | 94 | 4 | 0.6-24 | 0.02 # |
| 123478-HxCDF | 80 | 4 | 0.4-48 | 100 | 7.9 | 4.3-17 | 0.002 |
| 123678- HxCDF | 76 | 3.5 | 0.4-13 | 100 | 5.6 | 2.3-12 | 0.03 |
| I-TEQ | 100 | 19 | 10-60 | 100 | 27.2 | 13-63 | 0.01 |
| Adj-TEQ | 96 | 16 | 8-51 | 100 | 23.9 | 11-56 | 0.009 |

* p-value for Wilcoxon Test for SF-1998 vs. SF-1988; # SF- 1998 greater than SF-1988

**Table 2. Major PCB and OCP concentrations (ng/g fat) in breast adipose tissue (1998).**

| Analyte | N | Median | Mean | SD | min | max |
|---|---|---|---|---|---|---|
| % Lipid | 48 | 72 | 65 | 20 | 10 | 88 |
| 153 | 48 | 152 | 171 | 146 | 44 | 1019 |
| 180 | 48 | 113 | 131 | 85 | 33 | 546 |
| 138 | 48 | 59 | 82 | 73 | 20 | 417 |
| 170 | 48 | 43 | 51 | 34 | 14 | 215 |
| 182/187 | 48 | 44 | 49 | 30 | 15 | 204 |
| 194 | 48 | 25 | 38 | 52 | 0 | 351 |
| 74 | 48 | 35 | 41 | 29 | 11 | 199 |
| 118 | 48 | 29 | 38 | 47 | 6 | 330 |
| 196/203 | 48 | 33 | 38 | 25 | 14 | 180 |
| 156 | 48 | 25 | 34 | 31 | 4 | 184 |
| 199 | 48 | 26 | 31 | 22 | 11 | 150 |
| 206 | 48 | 15 | 22 | 22 | 4 | 117 |
| 113/99 | 48 | 15 | 21 | 22 | 4 | 155 |
| 177 | 48 | 15 | 20 | 16 | 3 | 83 |
| DDE | 44 | 695 | 777 | 367 | 169 | 1700 |
| t-nonachlor | 46 | 95 | 129 | 118 | 20 | 560 |
| Oxychlordane | 46 | 45 | 60 | 47 | 12 | 260 |
| DDT | 35 | 35 | 48 | 46 | 8 | 260 |
| , -HCH | 41 | 35 | 45 | 45 | 1 | 216 |
| HCB | 46 | 36 | 45 | 29 | 9 | 170 |
| Dieldrin | 45 | 27 | 36 | 34 | 12 | 230 |