Influence of the Consumption of Fatty Baltic Sea Fish on Plasma Levels of Halogenated Environmental Contaminants in Latvian and Swedish Men

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We examined the influence of widely varied consumption of fatty fish from the Baltic Sea and of age on plasma concentrations of polychlorinated biphenyls (PCBs), polychlorobiphenyls (OH-PCBs), 2,2-bis(4-chlorophenyl)-1,1,1-trichloroethane (4,4´-DDT), 2,2-bis(4-chlorophenyl)-1,1-dichloroethane (4,4´-DDE), 2,2,4,4´-tetrabromodiphenyl ether (BDE-47), hexachlorobenzene (HCB), and pentachlorophenol (PCP) in Latvian and Swedish men. Both age and fish consumption were significantly correlated with the concentrations of ΣPCB, ΣOH-PCB, 4,4´-DDE, 4,4´-DDT, and HCB. In the case of BDE-47, no significant relationship with age was observed, and fish consumption had the largest relative effect on plasma concentrations of this contaminant. This relationship may be a result of exposure to BDE-47 having been more recent than that of PCBs and DDE, or because the half-life of BDE-47 may be shorter than that of PCB and DDE. Latvian men demonstrated higher plasma levels of DDE and DDT but lower levels of ΣPCB and PCP than did Swedish men. The corresponding levels of HCB and BDE-47 were similar in both countries. The Spearman’s rank correlation coefficient obtained by comparing the level of the metabolite 4-hydroxy-2,3,3´,4,4´,5-pentachlorobiphenyl (4-OH-CB107) to the combined levels of its parent compounds, 2,3,3´,4,4´-pentachlorobiphenyl (CB-105) and 2,3,3´,4,4´-5-pentachlorobiphenyl (CB-118), was higher than the median correlation coefficient obtained upon comparing the level of this metabolite to all other possible combinations of two PCB levels. No other increased correlation between metabolite and parent PCB concentration was observed.

Key words: endocrine disruptors, fish consumption, hexachlorobenzene, pentachlorophenol, polychlorobiphenyls, polychlorinated diphenyl ethers, thyroid hormone. Environ Health Perspect 108:1035–1041 (2000). [Online 10 October 2000] http://ehpnet1.niehs.nih.gov/docs/2000/108p1035-1041sjodin/abstract.html
risk of neurodevelopmental and reproductive toxicity and endocrine disruption in humans from dietary exposure to OHS has received increasing attention [18]. Similarly, potential risk for immunosuppression and cancer caused by OHS are of concern [19,20]. A prerequisite for conducting reliable epidemiologic studies designed to evaluate these risks is the availability of well-characterized OHS exposure markers.

The major objective of the present investigation was to relate OHS concentrations in the plasma of Latvian and Swedish men to fish consumption, age, and country of origin. In addition, this study was designed to determine the levels of the predominant OH-PCBs present in human blood and to compare these levels to those of the parent PCB congeners. Furthermore, the level of the more recent environmental contaminant BDE-47, the major PBDE congener present in environmental samples, was determined and compared to the levels of other major environmental pollutants known to be present in humans.

Materials and Methods

Chemicals. The reference compounds used for preparation of standard solutions, their abbreviations, and their sources of origin are listed in Table 1. The internal surrogate standards used were CB-189 for quantitation of PCBs, 4,4´-DDE, 4,4´-DDT, and HCB; 4-OH-CB193 for quantitation of OH-PCBs; and 2,3,4-trichlorophenol (2,3,4-triCP) for quantitation of PCP. A volumetric standard BDE-128 was added for quantitation of BDE-47.

Hexane (distol grade; Fisher Scientific, Leicestershire, UK); methyl tert-butyl ether (MTBE; HPLC grade; Rathborn, Walkerburn, Scotland); 2-propanol [analytical (p.a.) grade; Prolabo, Cedex, France]; silica gel 60 (0.063–0.200 mm), sulfuric acid, and hydrochloric acid (p.a. grade; Merck, Darmstadt, Germany); and potassium hydroxide (p.a. grade; Eka Nobel, Bohus, Sweden) were used. Dianethane, used for derivatization of phenolic compounds, was prepared from N-methyl-N-nitroso-p-толуейлсуонамид (Dielsald) (24) obtained from Sigma-Aldrich (Steinheim, Germany).

Instrumentation. Gas chromatography with electron capture detection (GC-ECD) was performed on a Varian 3400 gas chromatograph (Varian, Walnut Creek, CA, USA) using a DB-5 capillary column (30 m × 0.25 mm i.d., 0.25 μm phase thickness; J&W Scientific, Folsom, CA, USA). Hydrogen was used as the carrier gas and nitrogen as the make-up gas. Injections were performed in the splitless mode. The column oven temperature was programmed as follows: 80°C (2 min), 10°C/min up to 300°C (5 min). The injector and detector temperatures were 250°C and 360°C, respectively. Data were collected and processed using a PC-based ELDSPro v1.0 system (Chromatographic Data System AB, Stockholm, Sweden).

Gas chromatography/mass spectrometry (GC/MS) was performed using a Finnigan TSQ 700 (ThermoQuest, Bremen, Germany) connected to a Varian 3400 gas chromatograph fitted with a DB-5HT capillary column (15 m × 0.25 mm i.d., 0.10 μm phase thickness; J&W Scientific) and with helium as the carrier gas. Splitless injections were performed at an injector temperature of 260°C. The column oven temperature was programmed as follows: 80°C (1 min), 15°C/min up to 300°C (10 min). The ion source temperature was 200°C and the pressure was 6.5 torr. The instrument was operated in the electron capture negative ionization (ECNI) mode with a primary electron energy of 70 eV. Selected ion monitoring (SIM) of the bromine isotopes m/z 79 and 81, was carried out (25). Methane (AGA, Stockholm, Sweden) of 99.995% purity and containing ≤ 5 ppm O₂ was used as the electron thermalization buffer gas.

Table 1. Reference compounds used for analyses of organohalogen substances in human plasma samples.

| Substance Abbreviation (PCBs) | Reference |
|------------------------------|-----------|
| 2,3,3,4,4´-Pentachlorobiphenyl  | CB-105    |
| 2,3,4,4´-Pentachlorobiphenyl    | CB-118    |
| 2,4,4´,5-Tetrachlorobiphenyl    | CB-129    |
| 2,2,3,3,4,5-Hexachlorobiphenyl  | CB-138    |
| 2,2,3,3,4,4´-Hexachlorobiphenyl | CB-146    |
| 2,2,4,4´,5,5´-Hexachlorobiphenyl| CB-153    |
| 2,3,3,4,4´-Hexachlorobiphenyl   | CB-156    |
| 2,3,4,4´-Hexachlorobiphenyl     | CB-157    |
| 2,2,2,3,3,4,5-Hexachlorobiphenyl| CB-167    |
| 2,2,2,3,4,4,4´-Heptachlorobiphenyl| CB-170 |
| 2,2,2,3,4,5,6-Heptachlorobiphenyl| CB-177 |
| 2,2,2,3,4,5,5´-Heptachlorobiphenyl| CB-180 |
| 2,2,2,3,4,5,6-Heptachlorobiphenyl| CB-183 |
| 2,2,2,3,4,5,5´-Heptachlorobiphenyl| CB-187 |
| 2,2,2,3,4,5,5´-Heptachlorobiphenyl (IS) | CB-189 |

Methoxy-PCBs

| Substance Abbreviation (PCBs) | Reference |
|------------------------------|-----------|
| 4-Methoxy-2,3´,4´,4,5-Pentachlorobiphenyl | 4-MeO-C8107 |
| 3-Methoxy-2,2´,3,4´,4,5-Hexachlorobiphenyl | 3-MeO-C8138 |
| 4-Methoxy-2,2´,3,4,4´,5-Hexachlorobiphenyl | 4-MeO-C8146 |
| 3-Methoxy-2,2´,4,4´,5,5´-Hexachlorobiphenyl | 3-MeO-C8153 |
| 4-Methoxy-2,2´,4,4´,5,5´,6-Heptachlorobiphenyl | 4-MeO-C8187 |
| 4-Methoxy-2,2´,3,4´,4,5,5´-Heptachlorobiphenyl (I.S.) | 4-MeO-C8193 |

Miscellaneous compounds

| Substance Abbreviation (PCBs) | Reference |
|------------------------------|-----------|
| 2,2,4,4´-Tetrabromodiphenyl ether | BDE-47 |
| 2,2,3,3,4,4´-Hexabromodiphenyl ether (I.S.) | BDE-128 |
| 1,1-dichloro-2,2-bis(4-chlorophenyl)ether | 4,4´-DDOE |
| 1,1-Trichloro-2,2-bis(4-chlorophenyl)ether | 4,4´-DDT |
| Hexachlorobenzene | HCB |
| 2,3,4-Trichlorophenol | 2,3,4-trCP |
| Pentachlorophenol | POP |

IS, internal surrogate standard.

*ProChem GmbH, Wesel, Germany. Synthesized as described. *Sigma-Aldrich Chemie GmbH, Steinheim, Germany. †Dr Ehrenstorfer GmbH, Augsburg, Germany. ‡Janssen Chimica, Beerse, Belgium. ‡Kebo, Stockholm, Sweden.
Concentration by a factor of less than 3. Reanalysis of selected samples, using a vol-
glass during preparation of these standards. Gate standards were observed to adsorb to
respectively. After the completion of the pre-
n, = 110) and 84% (CI, 57–86) of the
levels of 4,4´-DDT, whereas the
HC and BDE-47 levels did not differ signif-
icantly between the two countries. The variance explained by the three independent
variables (fish consumption, age, and coun-
try) varied for the different OHS between
29% and 62%, with 4,4´-DDT being the
lowest and ΣPCB the highest.

To investigate the age effect within each
fish consumption group in more detail, sepa-
rate multiple regression analyses for each
group were performed with respect to the
OHS studied, except PCP (data not shown).
Using this approach, influence of age on
plasma levels of these OHS was apparent
only in men with a high dietary intake of
fish. Weak age-related associations with
OHS levels among subjects with a lower fish
consumption cannot, however, be ruled out
because of the relatively small number of
subjects in each group. Age did not affect the
plasma levels of BDE-47, irrespective of the
levels of fish consumption. This lack of
effect of age on BDE-47 concentration is illus-
trated in Figure 1 and contrasted to the
influence of age on CB-153.

The correlation coefficient for the com-
parisons of 4-OH-CB107 with the sum level
of its potential parent compounds (CB-105
and CB-118; r = 0.70) was higher than the
median correlation of the 4-OH-CB107 level
to all possible sums of two PCB congeners
(\(r = 0.59\), 90th percentile, 0.70). In contrast,
other correlation coefficients between the
level of an OH-PCB to its potential parent
compound(s) (6,32) were all close to the
median correlation coefficient for each OH-
PCB to any other PCB or to all possible
combinations of two PCB congeners
[depending on whether these are one or two

Statistical evaluation. We used the
Mann-Whitney U-test to test group differ-
ces. Spearman’s rank correlation coeffi-
cients were calculated to compare the
concentrations of each OHS and fish con-
sumption and age. We performed multiple
regression analyses using the logarithms of
the OHS values, adjusting for fish consump-
tion, age, and country of origin. All p-values
< 0.05 were considered as significant.

Results

The plasma concentrations of 14 PCB con-
geners, 5 OH-PCBs, BDE-47, 4,4´-DDE,
4,4´-DDT, HCB, and PCP in Latvian and
Swedish males, stratified on fish consump-
tion habits, are presented in Table 3. With
the exception of PCP, the plasma concentra-
tions of all the OHS were significantly corre-
lated to the estimated fish consumption (r =
0.55–0.70). In contrast, PCP levels were
inversely correlated to fish consumption (r =
-0.37). Bivariate analyses revealed that age
was positively correlated with the levels of all
OHS (r = 0.26–0.51), again with the excep-
tion of PCP.

Multiple regression analysis including all
subjects confirmed a significant positive effect
of fish consumption on the plasma levels of
all OHS, except PCP (Table 4). The ΣPCB
level increased by 7% [95% confidence inter-
val (CI), 6–9] with each additional fish meal
per month. The most pronounced relative
impact of fish consumption was observed for
BDE-47, which increased by 13% (CI, 9–16)
with each additional fish meal per month.
The relative effects of fish consumption and
age on the levels of 4,4´-DDE, 4,4´-DDT,
and HCB were all similar to that observed for
ΣPCB. The association between age and
plasma level of BDE-47 observed in the
bivariate analysis was no longer seen when
the multivariate model was applied, but the
other age-related associations remained. The
ΣPCB levels increased by 2% (CI, 1–3) for
each additional year of age including all the
subjects. Multiple regression analysis revealed
that the plasma level of ΣPCB in Latvian
men was on average 70% (CI, 57–86) of
the corresponding Swedish level, whereas the
ΣOH-PCB levels in the Latvian and Swedish
samples did not differ. The levels of CB-105
and CB-118 were 66% (CI, 26–120) and
34% (CI, 5–72), respectively, higher in the
Latvian than in the Swedish males. Similarly,
the levels of 4-OH-CB107, a metabolite of
CB-105 and CB-118 (3,2), was 94% (CI,
42–165) higher in Latvian than in Swedish
males. The effects of country of residence on
the levels of the other individual PCB and
OH-PCB congeners studied were similar to
those observed in the case of ΣPCB and
ΣOH-PCB, respectively. Swedish men had
higher plasma levels of PCP but lower levels
of 4,4´-DDE and 4,4´-DDT, whereas the
HCB and BDE-47 levels did not differ sig-
ificantly between the two countries.

Table 2. Age and consumption of fatty fish from the Baltic Sea for the Latvian and Swedish males involved in the present study.

| Nationality and fish consumption groups | Age (years) | Fatty fish (meals/month) |
|----------------------------------------|-------------|--------------------------|
|                                        | Median      | Range        | Median | Range |
| Latvian                                |             |              |        |       |
| None or low                            | 19          | 43           | 27–64  | 0     | 0–1   |
| Moderate                               | 22          | 45           | 31–64  | 4     | 2–11  |
| High                                   | 26          | 55           | 24–79  | 19    | 13–32 |
| Swedish                                |             |              |        |       |
| None                                   | 20          | 37           | 23–62  | 0     | 0     |
| Moderate                               | 11          | 51           | 34–69  | 8     | 4–8   |
| High                                   | 12          | 48           | 23–63  | 16    | 12–20 |
potential parent PCBs; data not shown; i.e., 3'-OH-CB138 and CB-138; 3-OH-CB153 and CB-153; 4-OH-CB146 and Σ(CB-138, CB-153); and 4-OH-CB187 and Σ(CB-183, CB-187)]. Furthermore, in addition to the variation in 4-OH-CB107 levels discussed above, individual differences in the relative distribution of OH-PCB congeners were observed. This can be illustrated by the fact that the ratio of 3-OH-CB153/4-OH-CB146 concentration ranged from 0.15 to 0.80 (mean 0.27) for the Swedish population and from 0.15 to 0.80 (mean 0.27) for the Latvian population. This difference between the two countries was significant (p < 0.01).

Discussion

The present study was performed using blood samples drawn from men with different levels of consumption of fatty fish from the Baltic Sea. These samples were originally taken to investigate possible immunosuppression or endocrine disruption due to high consumption of fish contaminated with OHS (26–28), but no clearcut effects were observed. Even though these samples were obtained in the early 1990s, they are still suitable not only for determining OHS concentrations but also for examining the relative influence of fish consumption, age, and country of residence on these concentrations. Previous studies have shown that frequent consumption of fatty fish from the contaminated Baltic Sea results in higher plasma levels of OHS such as PCBs, 4,4'-DDE, and 4,4'-DDT (9).

The analytical procedure used was designed to quantitate both neutral and phenolic OHS. The cleanup was based on a procedure developed recently for the analysis of both of these classes of environmental contaminants in human blood (30). GC-ECD was used to quantitate all the compounds, with the exception of BDE-47, which, due to its low concentrations, had to be quantitated by GC/MS (ECN) (25).

The range of BDE-47 levels in the plasma of all individuals analyzed here was < 0.1–11 ng/g lipid weight, which can be compared to 22–2,300 ng/g lipid weight for the major PCB congener, CB-153. A recent study found median plasma levels of BDE-47 in female hospital cleaners and clerks from the south of Sweden (sampled in 1997) to be 1.6 and 1.5 ng/g lipid weight, respectively (39). Swedish mother’s milk from the same year has been reported to contain 2.3 ng BDE-47/g lipid weight (13), which is similar

### Table 3. Concentrations (ng/g lipid weight) of neutral and phenolic organohalogen compounds in the plasma of Latvian and Swedish men with different dietary consumptions of fatty fish from the Baltic Sea.

| Compound            | Latvia: None/low fish consumption | Latvia: Moderate fish consumption | Latvia: High fish consumption |
|---------------------|----------------------------------|----------------------------------|-------------------------------|
|                     | Median (10–90%)*                  | Median (10–90%)*                  | Median (10–90%)*              |
| Polychlorinated biphens |                                  |                                  |                               |
| CB-105              | 9 (4.4–16)                        | 6.3 (2.2–8.1)                    | 31.5 (6.2–32)                 |
| CB-118              | 43 (19–60)                        | 16 (7.4–51)                      | 100 (6.4–44)                  |
| CB-129              | 3.6 (2.2–8.1)                     | 9.8 (4.9–18)                     | 30 (19–41)                    |
| CB-138              | 120 (76–180)                      | 160 (80–300)                     | 360 (210–540)                 |
| CB-146              | 13 (7.2–22)                       | 16 (8.7–43)                      | 120 (60–210)                  |
| CB-153              | 160 (100–230)                     | 120 (60–230)                     | 360 (210–540)                 |
| CB-156              | 20 (12–29)                        | 24 (12–49)                       | 120 (60–210)                  |
| CB-157              | 5.9 (2.9–9.5)                     | 3.1 (1.5–7)                      | 43 (19–66)                    |
| CB-167              | 6.3 (3.8–11)                      | 5.5 (3.3–16)                     | 74 (30–180)                   |
| CB-170              | 31 (15–60)                        | 74 (37–120)                      | 160 (84–260)                  |
| CB-177              | 8.7 (5.3–12)                      | 21 (8.6–35)                      | 120 (64–210)                  |
| CB-180              | 74 (42–160)                       | 160 (84–260)                     | 360 (210–540)                 |
| CB-183              | 7.9 (5.7–13)                      | 18 (10–31)                       | 36 (13–27)                    |
| CB-187              | 34 (16–72)                        | 37 (16–76)                       | 56 (24–120)                   |
| ΣOCB               | 550 (340–890)                     | 780 (390–1,400)                  | 520 (380–2,200)               |
| Polychlorobiphenyls |                                  |                                  | 1,500 (1,200–2,800)           |
| 4-OH-CB107          | 82 (31–150)                       | 36 (15–110)                      | 3,000 (1,000–5,300)           |
| 3'-OH-CB138         | 18 (8.1–33)                       | 20 (7.5–45)                      | 1,600 (1,000–3,600)           |
| 4-OH-CB146          | 31 (17–62)                        | 39 (12–140)                      |                               |
| 3-OH-CB153          | 12 (7.3–28)                       | 15 (5.1–31)                      |                               |
| 4-OH-CB187          | 34 (23–61)                        | 74 (54–110)                      |                               |
| ΣOH-PCB            | 200 (105–290)                     | 190 (95–450)                     | 230 (110–1,000)               |
| Miscellaneous compounds |                                  |                                  | 350 (180–750)                 |
| BDE-47              | 0.26 (< 0.1–0.72)                 | 0.4 (< 0.1–2.5)                  | 230 (87–270)                  |
| 4,4'-DDE            | 660 (250–2,000)                   | 290 (140–900)                    | 58 (27–93)                    |
| 4,4'-DDT            | 40 (6.8–240)                      | 15 (5.1–68)                      | 43 (20–98)                    |
| HCB                | 71 (29–160)                       | 44 (25–81)                       | 42 (19–76)                    |
| PCB                | 610 (240–3,400)                   | 1,600 (600–5,000)                | 36 (26–67)                    |

*Percentile range. **Values corrected for interference present in blank samples.

### Table 4. The relative effects of age, fish consumption, and country of origin on the levels of organohalogen compounds in the plasma of Latvian and Swedish men as determined by multiple regression analysis.

| Compound | Fish consumption | Age | Country** | Adjusted R² |
|----------|------------------|-----|-----------|-------------|
| ΣOCB | exp(B) | 95% CI | p | exp(B) | 95% CI | p | exp(B) | 95% CI | p |
| 1.07 | 1.06–1.09 | < 0.001 | 1.02 | 1.01–1.03 | < 0.001 | 0.7 | 0.57–0.86 | < 0.001 | 0.62 |
| ΣOH-PCB | 1.06 | 1.04–1.08 | < 0.001 | 1.02 | 1.00–1.03 | 0.01 | 1.09 | 0.85–1.41 | 0.49 | 0.45 |
| BDE-47 | 1.13 | 1.09–1.16 | < 0.001 | 1.00 | 0.98–1.02 | 0.75 | 0.69 | 0.45–1.07 | 0.1 | 0.43 |
| 4,4'-DDE | 1.06 | 1.04–1.08 | < 0.001 | 1.02 | 1.01–1.04 | 0.01 | 1.37 | 1.01–1.86 | 0.05 | 0.45 |
| 4,4'-DDT | 1.04 | 1.02–1.07 | < 0.001 | 1.02 | 1.01–1.04 | 0.01 | 1.89 | 1.15–2.97 | 0.01 | 0.29 |
| HCB | 1.05 | 1.04–1.07 | < 0.001 | 1.01 | 1.00–1.03 | 0.02 | 1.25 | 0.97–1.60 | 0.08 | 0.44 |
| PCB | 0.98 | 0.96–0.99 | 0.01 | 1.00 | 0.99–1.02 | 0.68 | 0.38 | 0.29–0.51 | < 0.001 | 0.34 |

**Distinct variable, the value 1 was used for Latvia and 0 for Sweden.
to the levels obtained for the Latvian and Swedish men with no or low intake of fatty fish and lower than the levels of all other OHS. The largest relative effect of fatty fish consumption was observed for BDE-47, indicating that consumption of such fish is a major route of exposure for high consumers.

Meironyté et al. (13) found increasing levels of BDE-47 in human milk during the period 1972–1997, but the plasma levels of BDE-47 in the present study were not related to age, in contrast to PCBs and DDT (Figure 1, Table 4). The absence of an age-dependent increase in the plasma levels of BDE-47 (Figure 1) may be a reflection of the later introduction of PBDEs in the ecosystems. This is supported by increasing levels of BDE-47 in guillemot eggs from Stora Karlsö in the Baltic Sea until the early 1990s, after which the concentrations leveled off but showed large between-year variations (34). It is thus reasonable that the subjects in the present study were mainly exposed to BDE-47 during the years preceding the blood sampling, which diminishes the possibility of detecting an accumulation in body burden with age. Another possible explanation for the absence of any obvious age effect would be that BDE-47 has a much shorter half-life than that of CB-153, for example. Thus, a more rapid turnover of BDE-47 would lead to a steady-state situation that would be reached rather quickly, and no increase should be expected thereafter. However, BDE-47 seems to be a highly persistent PBDE congener because this is the major compound detected in all humans and wildlife analyzed, whereas other PBDE congeners are not (35). BDE-47 and 2,2,4,4,5-pentabromodiphenyl ether (BDE-99) are both present in similar concentrations in commercial PBDE products (36), but the latter is a minor constituent in biota (35).

The OHS found at highest levels in human plasma here was 4,4′-DDE, the highly persistent major metabolite of 4,4′-DDT. The plasma levels of 4,4′-DDT and 4,4′-DDE were strongly correlated with both fish consumption and age (Table 4). These two contaminants were also present in larger amounts in Latvian than in Swedish men. This finding is consistent with reports on 4,4′-DDE levels in perch from Latvian waters, which indicate local sources of this compound in the Riga area (37,38). The concentration of 4,4′-DDE in Swedish men with a low fish consumption observed here is comparable to the mean 4,4′-DDE level of 260 ng/g lipid weight in mother’s milk from the Stockholm region in 1991 (12). Considerably higher levels have been reported from areas where DDT is still in use, especially in developing countries (39). The population half-life of ΣDDT, calculated on the basis of published levels in human milk in countries where the use of DDT is either banned or restricted, is 4.2–5.6 years (39).

In the multiple regression analysis performed on each fish consumption group separately (data not shown), a significant effect of age on the levels of ΣPCB, 4,4′-DDE, 4,4′-DDT, and HCB remains for those with a high dietary intake of fatty fish from the Baltic Sea (compare the age-dependent increase in CB-153 level in the group with high fish consumption in Figure 1). No such effect was apparent among men with moderate or low consumption of fatty fish from the Baltic Sea. These observations indicate that the age effect is dependent on fish consumption (aging in combination with fish consumption results in increasing plasma levels of OHS). Furthermore, the rates of uptake and elimination seem to be similar in men with a moderate or low fish consumption, leading to a steady-state situation with respect to the levels of ΣPCB, 4,4′-DDE, 4,4′-DDT, and HCB. At the same time, it may be noted that the concentrations of these OHS in the fish consumed have decreased since the 1970s (8). This may have exaggerated the observed age effect because the older men have consumed fish with higher OHS concentrations than the younger men.

Whereas neutral lipophilic contaminants such as 4,4′-DDE are present in blood primarily as a consequence of equilibrium with lipid-rich tissues (40), PCP is mainly retained in the blood due to binding to albumin and TTR (41). The PCP level in plasma was inversely related to fish consumption and not affected by age, but was strongly correlated with the country in which the subjects lived, with the PCP levels being much lower in Latvia than in Sweden. Obviously, consumption of fish is not a major source of exposure to PCP. This conclusion is supported by the low concentration of this compound in fish muscle, in contrast to the higher concentrations seen in fish blood (7). Further, the group with low fish consumption demonstrated levels of PCP that were approximately 50% of the corresponding levels in Swedish men.

![Figure 1](image1.png) **Figure 1.** Plasma levels of (A) BDE-47 and (B) CB-153 in relationship to age for the three groups of men with different fish consumption: none or low (0–1 fish meals/month), moderate (2–11 fish meals/month), or high (> 12 fish meals/month). lw, lipid weight. Spearman’s rank correlation coefficients and levels of significance are $R_s = -0.03$, $p > 0.5$; $R_s = 0.00$, $p > 0.5$; and $R_s = 0.28$, $p = 0.10$ for BDE-47; and $R_s = 0.00$, $p > 0.5$; $R_s = 0.22$, $p > 0.20$; and $R_s = 0.71$, $p > 0.001$ for CB-153 for low, moderate, and high consumption, respectively.

![Figure 2](image2.png) **Figure 2.** Structures of the predominant polychlorobiphenylols present in human blood.
women in the early 1980s (16). HCB is metabolized to PCP to some extent, but this does not explain the high levels of PCP present in blood because the level of HCB was inversely correlated to that of PCP ($r_s = -0.29, p < 0.05$). Clearly, there must be other sources of PCP in the environment which remain to be identified. It can be speculated that exposure to PCP, due to its use as a wood preservative, occurs via indoor air (42). The use of PCP was banned in Sweden in 1975.

The present study has partly focused on determining the patterns and levels of OH-PCBs in the plasma of humans with different levels of fish consumption and, accordingly, different body burdens of PCB. Similar to PCP, OH-PCBs are retained in the blood plasma as a result of protein binding, primarily to TTR (15). The OH-PCB congeners are retained at relatively high concentrations compared to 2PCB in the blood (Table 3), even though the mechanism of accumulation is different. The PCB congeners are accumulated in the fat, whereas the OH-PCBs are bound to plasma proteins. The retention of a cluster of OH-PCBs in human plasma was first reported in 1994 (1/7). Additional information has since been presented (6), and recently an additional number of OH-PCB congeners present in human blood have been identified (43). A total of 30 OH-PCB congeners have been observed in human blood plasma (6), of which the five OH-PCB congeners (Figure 2) quantified here represent the major metabolites in human plasma.

The higher plasma levels of 4-OH-CB107 determined in Latvian men is most probably due to their higher plasma levels of the corresponding parent compounds CB-105 and CB-118, as indicated by the high correlation coefficient for the parent PCBs and OH-PCB metabolite. The other OH-PCB congeners quantified are formed from the more persistent PCB congeners, CB-138, CB-153, and CB-187, as shown by in vivo experiments (6,32). These latter PCB congeners were not observed to have better correlation coefficients than the median correlation of each OH-PCB to any other congener in the panel (17). The OH-PCB congeners are in the same range as the PCBs concentrations. Further work is in progress to determine the impact these PCB metabolites may have in humans and wildlife. The PBDE concentrations are much lower than those of PCBs and OH-PCBs, but because the levels seem to increase in humans (13), it is of concern that these are a serious contamination of the environment. Recently PBDEs and hydroxylated PBDEs have been indicated to have effects on the endocrine systems (49–51). More detailed knowledge is necessary to better assess the toxicological impact that this class of environmental contaminants may have.

In conclusion, consumption of fatty fish from the Baltic Sea has a significant influence on the plasma levels of neutral OHS and OH-PCBs, but not of PCP. The low plasma levels of BDE-47 observed were strongly related to fish consumption, which indicates a need for further information concerning dietary exposure of the population in the Baltic Sea region to PBDEs. An impact of fish consumption on plasma OH-PCB levels was also seen, and studies are now required to determine whether this represents a potential risk to human health.

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