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Polychlorinated Naphthalenes and Other Organochlorine Contaminants in Swedish Human Milk, 1972–1992

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Abstract. The concentrations of polychlorinated naphthalenes (PCNs) were determined together with polychlorinated biphenyls (PCBs), dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), 1,1-bis-(4-chlorophenyl)-2,2,2-trichloroethane (*p,p′*-DDT), 2,2-bis(4-chlorophenyl)-1,1-dichloroethylene (*p,p′*-DDE) and hexachlorobenzene (HCB) in milk, sampled in the course of 1972–92 from mothers living in Stockholm. A previously developed method for multicomponent analysis of organochlorine environmental contaminants was adapted for simultaneous analysis of PCNs. The mean recoveries of seven chlorinated naphthalene (CN) congeners added to milk prior to extraction were 76–99%. Similar recoveries were obtained for the commercial PCN product Halowax 1014. The pattern of PCNs in milk differed to a great extent from that in the commercial PCN products. The dominating congeners in breast milk were 1,2,3,5,7-pentachloronaphthalene (CN-52), 1,2,3,4,6,7- and/or 1,2,3,5,6,7-hexachloronaphthalene (CN-66/CN-67) and one unidentified tetrachloronaphthalene. There was a notable decrease in the concentrations of PCNs as was of the other organochlorine contaminants in milk from 1972 to 1992. During this time period the sum of CN congeners decreased from 3,081 to 483 pg/g milk fat and the sum of toxic equivalents of dioxin and dioxin-like compounds decreased from 100 to 39 pg/g milk fat.

During the last three decades a great number of investigations have shown the occurrence of environmental contaminants in human milk from different parts of the world (Jensen and Slorach 1990). Among the dominating persistent organochlorine compounds, pesticides such as DDT, its metabolite DDE, and HCB, the industrially used products polychlorinated biphenyls and the unintentionally produced polychlorinated dibenzo-*p*-dioxins and dibenzofurans have been previously reported in Swedish human milk (Norén 1988; Norén and Lundén 1991). Polychlorinated naphthalenes is another group of organochlorine compounds found in biota (Crookes and Howe 1993; Jansson *et al.* 1993), human blood plasma (Asplund 1994), and adipose tissue (Williams *et al.* 1993). PCNs have also been identified in human milk (Hayward *et al.* 1989), but not generally analyzed. The occurrence and toxicity of chlorinated naphthalene (CN) congeners has not been investigated to the same extent as of other organochlorine contaminants.

Since the beginning of this century, PCNs have had several industrial applications, *e.g.*, in cable insulations, engine oils, cutting and grinding fluids, wood preservatives and capacitors, and as replacement of PCBs. In Sweden the use of PCBs was restricted in 1972 and was only allowed in closed systems in capacitors and transformers until 1995 (Swedish Code of Statutes, SFS 1985:837, SFS 1988:1083). In other western countries the use of PCBs has virtually ceased (Ahlborg *et al.* 1992b). No restrictions have been applied for usage of PCNs in Sweden. However, at present no applications of PCNs are registered at the Swedish National Chemicals Inspectorate.

Organochlorine aromatic compounds are potentially toxic. The biological effects include, *e.g.*, loss of body weight, chloracne, thymic atrophy, carcinogenesis, teratogenesis, impaired immune response, and disturbances in reproduction. The subject has been extensively reviewed in Kimbrough (1980), Ahlborg *et al.* (1992a), and Safe (1994) among others. The induction of certain enzymes correlated to toxic effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) has also been shown for certain chlorinated biphenyls (CBs), for commercial PCN products (Cockerline *et al.* 1981) and highly chlorinated CN congeners (Campbell *et al.* 1983; Hanberg *et al.* 1990; Engwall *et al.* 1994). PCBs and PCNs have been observed to affect the antioxidative system and increase lipid peroxidation in rat liver (Mäntylä and Ahotupa 1993). Dioxins and some of PCBs have been reported to interfere with endocrine as well as immune systems (Birnbaum 1994). For example, in pregnant women and their newborn children, elevated levels of dioxins and CB congeners have been reported to alter the thyroid hormone status (Koopman-Esseboom *et al.* 1994). Several signs of poisoning, *e.g.*, lower birth weight and hyperpigmentation of skin and nails, have been reported in infants born to mothers accidentally exposed to higher levels of PCBs and PCDFs through contaminated rice oil in Japan and Taiwan. These children also demonstrated developmental delay, poorer performance on intelligence tests (Rogan *et al.* 1988), and memory deficits (Ko *et al.* 1994). Studies in the USA on toxic effects of PCBs to infants of the general population (Rogan *et*

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al. 1986) and of mothers consuming contaminated fish (Jacobson *et al.* 1990) indicated that neonatal exposure to PCBs in slightly elevated concentrations had adverse effects on neurological development, fetal and postnatal growth, and memory functions. Also in The Netherlands, higher levels of PCBs, PCDDs, and PCDFs in mothers were related to reduced neonatal neurological development of the infants; higher levels of planar PCBs were associated with a higher incidence of hypotonia (Huisman *et al.* 1995). In animal experiments low chlorinated *ortho*-substituted CBs have been shown to act as neurotoxicants (Eriksson and Fredriksson 1996).

For the general population, food is the main source of exposure to lipophilic persistent organochlorine compounds and lactation is the most important route of excretion in women. Since milk is an important form of nourishment for newborn children, the presence of contaminants in milk has raised concern about possible health risks in a breast-fed infant. The present study was undertaken to investigate the occurrence and time trends of PCNs and other organochlorine compounds in human milk by using a method for multicomponent analysis.

Materials and Methods

Samples

Pooled samples of human milk from healthy native Swedish mothers living in the Stockholm region were analyzed. The milk was collected during different periods from 1972 to the end of 1992 by the Mothers' Milk Centre in Stockholm. Equal amounts of milk from 10–20 mothers were mixed and stored at −20°C. The archived samples were pooled by mixing equal amounts of samples from the same time period. The average age of the mothers donating milk was 27–28 years in all time periods, except for 1988–89 and 1992, when the average age was 30 and 29 years, respectively. In each period of time, 55–60% of the mothers who supplied milk were nursing their first infant. The majority of the rest were nursing their second child.

Standards

The commercial products Halowax 1014 and Clophen A50 were from Koppers Co., Pittsburgh, PA, USA and Bayer AG, Leverkusen, Germany, respectively. $^{13}C_{12}$-labeled congeners of PCDDs, PCDFs, and PCBs (numbering of PCBs according to Ballschmiter *et al.* 1993): 2,3,7,8-TCDD; 1,2,3,7,8-PeCDD; 1,2,3,6,7,8-HxCDD; 1,2,3,4,6,7,8-HpCDD; OCDD; 2,3,7,8-TCDF; 1,2,3,7,8-PeCDF; 1,2,3,4,7,8-HxCDF; 1,2,3,4,6,7,8-HpCDF; OCDF; 3,3′,4,4′-TeCB (CB-77); 3,3′,4,4′,5-PeCB (CB-126); and 3,3′,4,4′,5,5′-HxCB (CB-169) were from Cambridge Isotope Laboratories Inc., Woburn, MA, USA. The unlabeled PCDD and PCDF congeners were obtained from WHO interlaboratory quality control study 1991. Unlabeled CB congeners were from Riedel-de Haën AG, Seelze, Hannover, Germany, Dr. Ehrenstorfer, Augsburg, Germany, and Cambridge Isotope Laboratories Inc., Woburn, MA, USA. The following congeners of CB and CN (numbering of PCNs according to Wiedmann and Ballschmiter 1993): 2,3,3′,4,4′-PeCB (CB-105); 2,3′,4,4′,5-PeCB (CB-118); 2,3,3′,4,4′,5-HxCB (CB-156); 2,3,3′,4,4′,5′-HxCB (CB-157); 1,2,3,4,6,7-HxCN (CN-66)/1,2,3,5,6,7-HxCN (CN-67); 1,2,4,5,6,8-HxCN (CN-71); 1,2,3,4,5,6,7-HpCN (CN-73); and 1,2,3,4,5,6,7,8-OCN (CN-75) were kind gifts from Åke Bergman, Stockholm University, synthesized as reported (Sundström 1973; Haglund and Bergman 1989; Bergman *et al.* 1990; Jakobsson *et al.* 1992, 1994). The PCN congeners: 1,2,5,6-TeCN (CN-36), 1,2,3,5,7-PeCN (CN-52), and 1,2,3,4,5,6-HxCN (CN-63) were purchased from Larodan Fine Chemicals AB, Malmö, Sweden. Hexachlorobenzene (HCB) was from Dr. Ehrenstorfer, Augsburg, Germany, and the following pesticides: 2,2-bis-(4-chlorophenyl)-1,1-dichloroethylene (*p,p′*-DDE); 1,1-bis-(4-chlorophenyl)-2,2,2-trichloroethane (*p,p′*-DDT); 1-(2-chlorophenyl)-1-(4-chlorophenyl)-2,2,2-trichloroethane (*o,p′*-DDT); and 1,1-bis-(4-chlorophenyl)-2,2-dichloroethane (*p,p′*-DDD) were from Geigy AG, Basel, Switzerland.

Extraction and Purification

Due to the general occurrence of PCBs and PCNs, precautions must be taken to avoid contamination of the samples. The solvents were of HPLC or *pro analysi* quality and redistilled prior to use (Norén *et al.* 1996). The solvents and blank samples were controlled for occurrence of contaminants. All glassware was carefully cleaned with different solvents, washed in an ultrasonic bath, and heated at 280°C. Prior to use the glassware was rinsed with n-hexane.

Two milk samples (10 ml) and one blank sample (10 ml of water) were extracted and purified in parallel (Norén *et al.* 1996). The samples were extracted with the lipophilic gel Lipidex 5000 according to Norén and Sjövall (1987). Prior to extraction $^{13}C_{12}$-labeled internal standards were added to all samples. Additional unlabeled standards were added to one of the milk samples and run in parallel to perform recovery studies. Purification and separation of the chlorinated compounds into different groups were achieved by chromatography using aluminium oxide, silica gel, basic aluminium oxide (Norén and Sjövall 1987), and activated charcoal (Norén *et al.* 1990; Weistrand *et al.* 1995).

Identification and Quantification

Pesticides, mono-*ortho*-, and di-*ortho*-substituted CBs were quantified by capillary gas chromatography using a Pye Unicam GCV instrument equipped with a ^{63}Ni electron capture detector, an all-glass falling-needle injector, and a fused silica capillary column coated with methyl phenyl (5%) silicone (25 m × 0.32 mm I.D., 0.25 µm film thickness, Quadrex, New Haven, CT, USA). Total PCBs were analyzed according to the original method using a packed column (Norén *et al.* 1990). CB-15 was used as an injection standard.

The congener-specific determinations of mono-*ortho*- and non-*ortho*-substituted CBs, PCNs, PCDDs, and PCDFs were made by a VG 70-250 mass spectrometer (Micromass, Manchester, UK) equipped with an HP 5890A gas chromatograph and a VG-250 data system. A fused silica capillary column (see above) was used with helium as carrier gas. An all-glass, falling-needle injector was used with an injector heater at 260°C.

Electron ionization was performed in an ''EI only'' ion source at a temperature of 260°C, an electron energy of 30 eV and a trap current of 500 µA. The resolution at m/z 293 was 7,000–9,000 at an accelerating voltage of 6 kV. The mass spectrometer was operated in a selected ion recording mode. Two ions of the molecular cluster were recorded. Ions from perfluorokerosene were used as reference masses for correction of mass spectrometer drift (lock mass). CB-209 was used as an injection standard.

Results

Polychlorinated Naphthalenes

The previously used methods for analysis of organochlorine compounds in human milk (Norén and Sjövall 1987) were

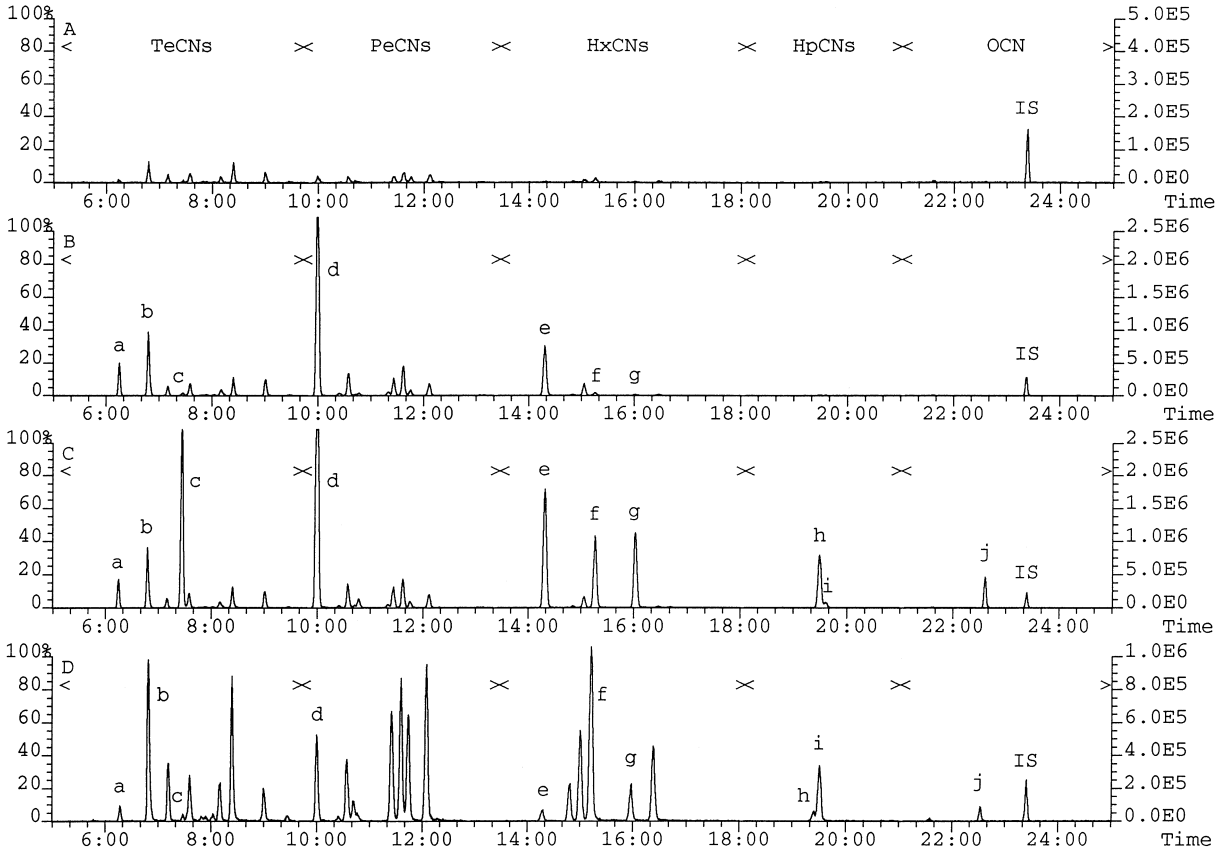

Fig. 1. Selected ion-current chromatograms of TeCN (m/z 265.9038), PeCN (m/z 299.8648), HxCN (m/z 335.8228), HpCN (m/z 369.7839), OCN (m/z 403.7449), and CB-209 (m/z 427.7449). The chromatograms were obtained from a blank sample (A), human milk (B), human milk with added CN congeners (C) and Halowax 1014 (D). Marked peaks are TeCN No. 1 (a), TeCN No. 2 (b), CN-36 (c), CN-52 (d), CN-66/CN-67 (e), CN-71/CN-72 (f), CN-63 (g), CN-73 (h), CN-74 (i), CN-75 (j), and CB-209 (IS)

adapted for simultaneous analysis of PCNs. Recovery studies were made by addition of 100–278 pg of CN-36, CN-52, CN-66/CN-67, CN-71, CN-63, CN-73, and CN-75 to 10 ml milk (Figure 1). Of the standard compounds, two isomers, 1,2,3,4,6,7-HxCN (CN-66) and 1,2,3,5,6,7-HxCN (CN-67), were obtained as a mixture. These isomers were formed as a mixture of equal amounts in the synthesis (Jakobsson *et al.* 1992). The presently used fractionation steps and GC column did not separate the two isomers and, therefore, they were calculated as one compound. The mean recoveries of individual PCN congeners were 76–99% (n = 8; total range 60–104%). Similar recoveries were obtained for the technical product of PCNs, Halowax 1014. The last of the TeCN peaks (Figure 1) and occasionally 1,2,3,4,5,6,7-HpCN (CN-73) were not completely fractionated on the basic aluminium oxide column. However, this did not create any problem in the investigation because the last TeCN, CN-73 and 1,2,3,4,5,6,8-HpCN (CN-74) as well as 1,2,3,4,5,6,7,8-OCN (CN-75) were not present in the milk.

The pattern of PCN congeners in human milk differed considerably from the technical product (Figure 1). The concentrations given in Table 1 are corrected for levels in the blank sample, which was extracted and purified in parallel. Since $^{13}C_{12}$-labeled CN congeners were not available to be used as internal standards, the concentrations of CNs were corrected by the mean recovery of the HxCNs (CN-66/CN-67, CN-63, and CN-71) added to the milk sample run in parallel. These values agreed with the values obtained then $^{13}C_{12}$-labeled CB-169 (added to all samples) was used as an internal standard in the quantification of PCN congeners.

During the time period studied, the sum of CNs has declined in breast milk by 84%, from 3,081 pg/g fat (1972) to 483 pg/g fat (1992) (Table 1). A congener with five chlorine atoms, CN-52 was the most abundant, followed by the two with six, CN-66/CN-67, and two with four chlorine atoms, TeCN No. 2 and TeCN No. 1 (Figure 2). These congeners constituted on an average 51, 19, 19, and 9%, respectively, of the sum of CNs.

Polychlorinated Biphenyls

The investigation included the CB congeners recommended to be analyzed in priority according to the Nordic Risk Assessment of PCBs (Ahlborg *et al.* 1992b). Mono-*ortho*-substituted CBs present in small amounts close to the detection limit in determination by GC-ECD, were confirmed by GC-MS selected ion recording after fractionation on a charcoal column. The isomers CB-170 and CB-190 coeluted from the GC-column and the peak was quantified as CB-170.

The levels of total PCBs have declined by 65% from 1972 (1,090 ng/g fat) to 1992 (380 ng/g fat) (Table 2). Lower chlorinated congeners (*e.g.* CB-28 and CB-105) decreased

Table 1. Average concentrations (pg/g fat) of PCN congeners and non-*ortho*-substituted PCBs in Swedish human milk (ranges are given in italics)

Year	1972	1976	1980	1984–85	1988–89	1990	1991	1992
No. of mothers	75	78	116	102		60	60	40
No. of pooled samples	1	1	1	2		3	3	2
Lipids, %	2.8	2.7	3.0	2.5		2.5	2.4	2.7
				2.4–2.5		*2.4–2.6*	*2.0–2.6*	*2.5–2.8*
TeCN no. 1	346	119	84	94	NA	58	39	37
				87–100		*40–68*	*34–42*	*24–50*
TeCN no. 2	791	269	147	238	NA	119	84	77
				209–267		*75–158*	*63–102*	*21–133*
CN-36	22	11	ND	13	NA	ND	ND	ND
1,2,5,6-TeCN				*8–17*				
CN-52	1,439	1,004	691	344	NA	350	283	261
1,2,3,5,7-PeCN				*276–413*		*218–513*	*226–361*	*112–409*
CN-66/CN-67[1]	438	310	252	159	NA	175	92	103
1,2,3,4,6,7-/1,2,3,5,6,7-HxCN				*100–218*		*111–216*	*73–103*	*63–142*
CN-71/CN-72[2]	36	12	38	38	NA	9	3	5
1,2,4,5,6,8-/1,2,4,5,7,8-HxCN				*9–66*		*0–28*	*0–9*	*0–10*
CN-63	9	7	18	ND	NA	ND	ND	ND
1,2,3,4,5,6-HxCN								
Sum of PCNs	3,081	1,732	1,230	886	NA	711	501	483
No. of mothers	195	204	431	102	140	60	60	40
No. of pooled samples	3	3	4	2	7	3	3	2
Lipids, %	2.7	2.7	2.9	2.8	2.6	2.5	2.4	2.8
	2.6–2.8	*2.7–2.8*	*2.9–3.1*	*2.6–2.9*	*2.2–2.9*	*2.4–2.7*	*2.0–2.6*	*2.7–2.8*
CB-77	76	41	29	35	27	26	20	24
3,3′,4,4′-TeCB	*65–88*	*27–62*	*27–33*	*34–36*	*19–47*	*24–28*	*17–22*	*19–30*
CB-126	298	253	166	102	98	117	86	104
3,3′,4,4′,5-PeCB	*260–355*	*226–297*	*141–183*	*91–114*	*78–122*	*110–128*	*68–98*	*91–117*
CB-169	67	74	65	43	47	59	41	56
3,3′,4,4′,5,5′-HxCB	*66–69*	*71–78*	*59–77*	*38–48*	*40–54*	*56–62*	*38–42*	*52–61*

NA = not analyzed; ND = not detected <1 pg/g fat
[1] CN-66 and CN-67 are not separated
[2] CN-71 and CN-72 are not separated

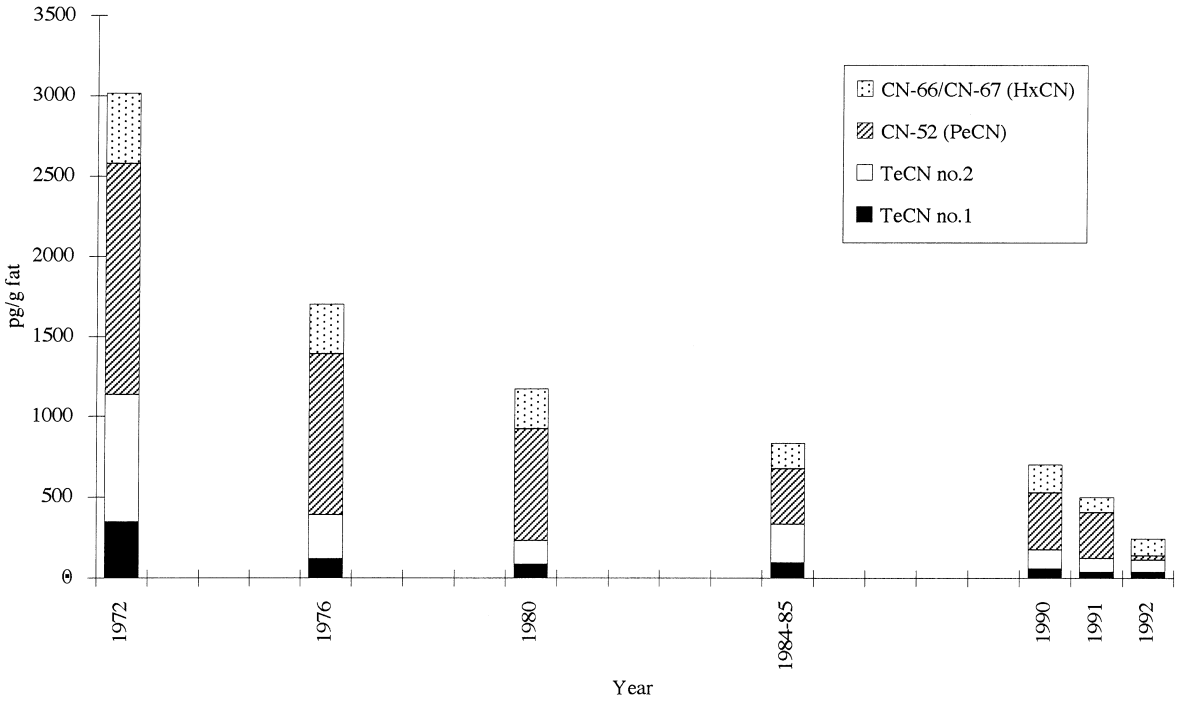

Fig. 2. Average concentrations (pg/g fat) of chlorinated naphthalenes in Swedish breast milk during the period 1972–1992

Table 2. Average concentrations (ng/g fat) of PCBs and pesticides in Swedish human milk (ranges are given in italics)

Year	1972	1976	1980	1984–85	1988–89	1990	1991	1992
No. of mothers	135	153	431	102	120	60	60	40
No. of pooled samples	2	2	4	2	6	3	3	2
Lipids, %	2.8	2.9	3.0	2.8	2.7	2.5	2.4	2.8
	2.7–2.9	*2.8–3.0*	*2.9–3.1*	*2.6–2.9*	*2.3–3.1*	*2.4–2.7*	*2.0–2.6*	*2.7–2.8*
CB-28	34	22	29	22	9	9	6	4
2,4,4′-TrCB	*33–36*	*20–25*	*18–40*	*19–25*	*5–14*	*6–12*	*5–7*	*4–4*
CB-47	ND	NA	NA	NA	NA	ND	ND	ND
2,2′,4,4′-TeCB								
CB-52	4[1]	24[x]	20[x]	14[x]	24[x]	1	1	1
2,2′,5,5′-TeCB						*1–1*	*1–1*	*1–1*
CB-101	11[1]	NA	NA	NA	NA	2	2	2
2,2′,4,5,5′-PeCB						*2–2*	*1–2*	*1–2*
CB-105	15	16	8	8	7	5	4	3
2,3,3′,4,4′-PeCB	*14–15*	*15–18*	*6–8*	*7–8*	*4–7*	*4–5*	*3–4*	*3–3*
CB-114	1[1]	1[2]	1[3]	1	NA	1[5]	1	1[5]
2,3,4,4′,5-PeCB				*1–2*			*1–1*	
CB-118	60	46	31	24	25	19	16	15
2,3′,4,4′,5-PeCB	*56–64*	*44–48*	*22–34*	*24–24*	*23–30*	*18–20*	*14–19*	*14–16*
CB-122	ND	NA	NA	NA	NA	ND	ND	ND
2′,3,3′,4,5-PeCB								
CB-138	190	177	134	108	112	87	74	62
2,2′,3,4,4′,5′-HxCB	*188–191*	*173–181*	*102–174*	*104–113*	*99–122*	*84–91*	*64–80*	*58–67*
CB-153	215	197	152	124	146	116	106	96
2,2′,4,4′,5,5′-HxCB	*211–219*	*193–201*	*114–188*	*118–130*	*128–153*	*110–122*	*104–109*	*90–102*
CB-156	20	19	13	12	13	13	9	10
2,3,3′,4,4′,5-HxCB	*20–20*	*18–20*	*10–16*	*12–13*	*11–15*	*11–16*	*9–10*	*9–10*
CB-157	4[1]	3[2]	2[3]	2[4]	NA	3	2	2
2,3,3′,4,4′,5′-HxCB						*2–3*	*2–2*	*2–2*
CB-167	11[1]	4[2]	3[3]	4	NA	5	4	3[5]
2,3′,4,4′,5,5′-HxCB				*2–6*		*4–6*	*4–4*	
CB-170/CB-190	41[1]	NA	NA	23[6]	NA	26	24	20[5]
2,2′,3,3′,4,4′,5-/2,3,3′, 4,4′,5,6-HpCB						*24–28*	*22–26*	
CB-180	88	84	65	53	67	51	48	40
2,2′,3,4,4′,5,5′-HpCB	*82–93*	*80 –88*	*44–85*	*49–57*	*61–71*	*50–53*	*44–50*	*36–44*
Total PCBs	1090	910	780	600	650	510	410	380
	1080–1100	*900–920*	*720–900*	*520–690*	*530–710*	*480–530*	*380–430*	*340–420*
p,p′-DDE	2500	1500	1055	500	480	369	255	227
	2300–2700	*1300–1700*	*880–1150*	*380–580*	*300–680*	*354–395*	*206–288*	*203–251*
p,p′-DDT	690	340	185	61	47	42	36	22
	630–750	*320–360*	*160–190*	*44–70*	*26–78*	*32–50*	*34–40*	*13–32*
o,p′-DDT	NA	NA	NA	NA	NA	4	2	3
						3–4	*2–3*	*2–4*
p,p′-DDD	NA	NA	NA	NA	NA	ND	ND	ND
HCB	130	110	125	37	40	33	27	31
	120–140	*110–110*	*90–180*	*29–43*	*29–51*	*30–36*	*26–30*	*26–36*

ND = not detected = <1 ng/g fat; NA = not analyzed

[x] Interference possible

One pooled sample from [1] 75; [2] 78; [3] 116; [4] 26; [5] 20; [6] 76 mothers

more rapidly than higher chlorinated (*e.g.* CB-153, CB-156, and CB-180). There was also a marked difference in the decline of non-*ortho*-substituted coplanar CBs as seen in Table 1; there the concentrations for 1990–92 are given together with previously reported levels (Norén and Lundén 1991). In 1992 the concentrations of CB-77 and CB-126 were about 30% of the levels in samples from 1972. The level of CB-169 was more constant and in 1992 was still 84% of that in 1972, indicating a difference in accumulation/excretion of the congeners.

Pesticides

The reported decline in the levels of HCB, *p,p′*-DDT, and *p,p′*-DDE from 1972 to 1989 has continued (Table 2) (Norén 1988). However, from 1984 on, only small differences are observed in the concentration of HCB, which was 31 ng/g fat in 1992 corresponding to 24% of that in 1972. The concentrations of *p,p′*-DDT and *p,p′*-DDE were in 1992 only 3% (22 ng/g fat) and 9% (227 ng/g fat), respectively, of the levels in 1972.

o,p′-DDT and *p,p′*-DDD were included in the analyses of samples from 1990–92. Detectable levels (2–4 ng/g lipids) were found only for *o,p′*-DDT (Table 2).

Polychlorinated Dibenzo-p-*dioxins and Dibenzofurans*

One pooled sample from 1972 was reanalyzed and quantified for PCDDs and PCDFs together with the samples from 1990–92 and additional congeners were included (Table 3). The concentrations in the reanalyzed sample agreed with previously reported data from 1972 (Norén 1988). No baseline separation was obtained of 1,2,3,4,7,8- and 1,2,3,6,7,8-HxCDD on the GC column and these isomers were therefore calculated as one compound. The ratio of 1,2,3,4,7,8- and 1,2,3,6,7,8-HxCDD was estimated to be 1:15. During the years from 1972 to the end of 1992 the concentrations of PCDD and PCDF congeners in Swedish breast milk (Table 3) have decreased by 30–61% and 67–86%, respectively, except for HpCDD (76%) and TCDF (33%).

Toxic Equivalents

Toxic equivalency factors (TEFs) refer to the relative toxicities of dioxin-like compounds in relation to 2,3,7,8-TCDD. Such factors have been proposed for compounds with structural relationship to the PCDDs and PCDFs, which bind to the A*h*-receptor and elicit dioxin-specific biochemical and toxic responses (Ahlborg *et al.* 1994). In the present study toxic equivalents (TEQs) were calculated by using TEFs proposed for PCDD/PCDF in the Nordic risk assessment of dioxins (Ahlborg *et al.* 1988) and for PCBs by WHO-ECEH/IPCS (Ahlborg *et al.* 1994). Several highly chlorinated PCN congeners have been shown to induce hepatic, microsomal, drug-metabolizing enzymes. The lateral substitution of chlorine at 2,3,6,7 positions was important for the activity, indicating a structure activity relationship similar to PCDDs, PCDFs, and PCBs (Campbell *et al.* 1983). Hanberg *et al.* (1990) compared the toxicity of certain PCN congeners, based on ethoxyresorufin *O*-deethylase (EROD) and aryl hydrocarbon hydroxylase (AHH) activity, with that of TCDD. The congeners CN-66/CN-67 and CN-63 were among the most potent, corresponding to the toxic response 0.002 relative to TCDD. This by Hanberg *et al.* proposed TEF (although not authorized by regulatory agencies) was included in the calculations (Table 4). The TEQ calculation is based on the assumption that the effects are additive. Calculations of TEQ values for PCDDs and PCDFs from the years 1976, 1980, and 1984–85, given in Table 4, are based on concentrations reported previously (Norén 1988). Because the TEFs for PCBs have been revalued (Ahlborg *et al.* 1994), the TEQs in Table 4 are not identical with the previously reported data (Norén and Lundén 1991).

The main contribution to the sum of TEQs in Swedish human milk was from CB-126 (on average 29%), followed by 2,3,4,7,8-PeCDF (18%) and CB-156 (13%) (Table 4). The contribution from CN-66/CN-67 to the sum of TEQs was on the same level as that from the coplanar CB-169 (Table 4). The total TEQs have decreased by 61% from 100 pg/g fat in 1972 to 39 pg/g fat in 1992. A tolerable weekly intake (TWI) of 0–35 pg TCDD equivalents/kg body weight has been proposed in the Nordic risk assessment of dioxins (Ahlborg *et al.* 1988). Including the TEQs of dioxin-like compounds and assuming that an infant with a body weight of 5 kg consumes 700 ml milk/day, it can be seen that an infant on an average exceeded the tolerance level by a factor of about 80 in 1972 and by 30 in 1992. However, the proposed TWI assumes lifelong intake and cannot be directly compared with the time-limited intake of milk by an infant (Ahlborg *et al.* 1988).

Table 3. Average concentrations (pg/g fat) of PCDDs and PCDFs in Swedish human milk (ranges are given in italics)

Year	1972	1990	1991	1992
Number of mothers	75	60	60	40
Number of pooled samples	1	3	3	2
Lipids, %	2.6	2.5	2.4	2.7
		2.5–2.6	*2.0–2.6*	*2.7–2.8*
2,3,7,8-TCDD	5	3	2	3
		2–3	*1–2*	*2–3*
1,2,3,7,8-PeCDD	12	4	4	6
		4–5	*3–6*	*5–7*
1,2,3,4,7,8- and 1,2,3,6,7,8-HxCDD	42	27	20	27
		21–35	*19–21*	*24–30*
1,2,3,7,8,9-HxCDD	10	6	5	7
		5–7	*3–6*	*6–8*
1,2,3,4,6,7,8-HpCDD	164	44	35	40
		37–56	*31–37*	*38–42*
OCDD	592	345	222	232
		289–442	*217–231*	*208–257*
Sum of PCDDs	825	429	288	315
2,3,7,8-TCDF	3	2	1	2
		1–2	*1–1*	*1–2*
1,2,3,7,8-PeCDF	2	<1	<1	<1
2,3,4,7,8-PeCDF	43	14	11	14
		12–20	*9–12*	*10–17*
1,2,3,4,7,8-HxCDF	13	3	3	3
		3–4	*3–3*	*3–4*
1,2,3,6,7,8-HxCDF	11	4	3	3
		3–6	*2–3*	*3–4*
2,3,4,6,7,8-HxCDF	5	2	2	1
		2–2	*2–2*	*0–2*
1,2,3,7,8,9-HxCDF	<1	<1	<1	<1
1,2,3,4,6,7,8-HpCDF	49	6	5	7
		5–8	*5–5*	*5–8*
1,2,3,4,7,8,9-HpCDF	2	<1	<1	<1
OCDF	4	<4	3	<4
			2–3	
Sum of PCDFs	132	31	28	30

Discussion

The previously used multicomponent method was shown to be applicable for determination of PCN in breast milk. However, it was obvious from the recovery studies, that for a proper elution of PCNs the last methanol/water fraction from the Lipidex gel has to be completely drained off prior to elution with acetonitrile (Norén and Sjövall 1987). Otherwise, the eluting solvent will be too polar, leading to retention of PCNs in the gel.

Seven congeners of CN were found in the milk samples (Table 1). The sum of these was 0.1–0.3% of the total PCB

Table 4. TEQs in Swedish human milk, expressed as pg/g fat

		TEQs (pg/g fat)						
Year	TEFs	1972	1976	1980	1984–85	1990	1991	1992
Non-*ortho*-substituted PCBs								
CB-77	0.0005	0.038	0.020	0.014	0.018	0.013	0.010	0.012
CB-126	0.1	29.8	25.3	16.6	10.2	11.7	8.6	10.4
CB-169	0.01	0.67	0.74	0.65	0.43	0.59	0.41	0.56
Σ		31	26	17	11	12	9	11
Mono-*ortho*-substituted PCBs								
CB-105	0.0001	1.5	1.6	0.8	0.8	0.5	0.4	0.3
CB-114	0.0005	0.5	0.5	0.5	0.5	0.5	0.5	0.5
CB-118	0.0001	6.0	4.6	3.1	2.4	1.9	1.6	1.5
CB-156	0.0005	10.0	9.5	6.5	6.0	6.5	4.5	5.0
CB-157	0.0005	2.0	1.5	1.0	1.0	1.5	1.0	1.0
CB-167	0.00001	0.1	0.04	0.03	0.04	0.05	0.04	0.03
Σ		20	18	12	11	11	8	8
Di-*ortho*-substituted PCBs								
CB-170	0.0001	4.1	NA	NA	2.3	2.6	2.4	2.0
CB-180	0.00001	0.88	0.84	0.65	0.53	0.51	0.48	0.40
Σ		5			3	3	3	2
Σ PCBs		56	44	29	25	26	20	21
PCNs								
CN-66/CN-67	0.002	0.88	0.62	0.50	0.32	0.35	0.18	0.21
CN-63	0.002	0.02	0.01	0.04	ND	ND	ND	ND
Σ		0.9	0.6	0.5	0.3	0.4	0.2	0.2
PCDDs								
2,3,7,8-TCDD	1.0	5.0	5.0	3.0	1.0	3.0	2.0	3.0
1,2,3,7,8-PeCDD	0.5	6.0	3.5	3.0	2.5	2.0	2.0	3.0
1,2,3,4,7,8-/1,2,3,6,7,8-HxCDD	0.1	4.2	4.0	3.1	3.0	2.7	2.0	2.7
1,2,3,7,8,9-HxCDD	0.1	1.0	NA	NA	NA	0.6	0.5	0.7
1,2,3,4,6,7,8-HpCDD	0.01	1.64	0.96	0.70	0.69	0.44	0.35	0.40
OCDD	0.001	0.59	0.37	0.34	0.24	0.34	0.22	0.23
Σ		18	14	10	7	9	7	10
PCDFs								
2,3,7,8-TCDF	0.1	0.3	0.3	0.3	0.2	0.2	0.1	0.2
1,2,3,7,8-PeCDF	0.01	0.02	NA	NA	NA	<0.01	<0.01	<0.01
2,3,4,7,8-PeCDF	0.5	21.5	14.5	8.5	7.0	7.0	5.5	7.0
1,2,3,4,7,8-HxCDF	0.1	1.3	NA	NA	NA	0.3	0.3	0.3
1,2,3,6,7,8-HxCDF	0.1	1.1	1.4	0.8	0.8	0.4	0.3	0.3
2,3,4,6,7,8-HxCDF	0.1	0.5	NA	NA	NA	0.2	0.2	0.1
1,2,3,7,8,9-HxCDF	0.1	<0.1	NA	NA	NA	<0.1	<0.1	<0.1
1,2,3,4,6,7,8-HpCDF	0.01	0.49	0.21	0.07	0.08	0.06	0.05	0.07
1,2,3,4,7,8,9-HpCDF	0.01	0.02	NA	NA	NA	<0.01	<0.01	<0.01
OCDF	0.001	0.004	0.004	0.005	0.005	<0.004	0.003	<0.004
Σ		25	16	10	8	8	6	8
Σ Total TEQs		100	75	50	40	43	33	39

NA = not analyzed; ND = not detected

TEFs are according to: Ahlborg *et al.* 1994 (PCBs), Hanberg *et al.* 1990 (PCNs) and Ahlborg *et al.* 1988 (PCDDs/PCDFs)

levels. In each group of isomers with 4–6 chlorine atoms, the early eluting congeners from the GC column were the most abundant (Figure 1). A similar pattern was found in an investigation of Swedish blood plasma (Asplund 1994), although considerably more congeners were reported. In the determination of 2,3,7,8-TCDF in Californian and Swedish human milk, Hayward *et al.* (1989) found interferences from PCNs. The levels of PCNs were estimated to be 10–100 times of that of PCDDs and PCDFs. In our present and previous investigations, PCDDs and PCDFs were separated from PCNs and PCBs (except the non-*ortho*-substituted CBs) by a basic aluminium oxide column and interferences in PCDD/PCDF analysis were not noticed. In adipose tissue from Canadians the levels of CN-66/CN-67 and an unknown PeCN ranged 0.1–2.4 ng/g fat and 0.1–25 ng/g fat, respectively (Williams *et al.* 1993). Furthermore, a DiCN has been identified in human milk (Newsome *et al.* 1995).

HpCNs and OCN were not found in the present investigation of milk. This is in accordance with the bioaccumulation pattern found in fish (Crookes and Howe 1993) and in rats after oral

administration of Halowax 1014 (Asplund *et al.* 1986, 1994). In rats a selective retention of CN-66/CN-67 was observed in the adipose tissue and liver. Most of the clinical observations, especially chloracne, as well as the available experimental data suggest that PeCNs and HxCNs are the most toxic congeners of the chlorinated naphthalenes (Kimbrough 1980). Accordingly, the occurrence of such compounds in human milk should be considered.

The previously reported (Norén and Lundén 1991) discontinuance in the decline of PCB levels from 1984 to 1989 seems to have passed and a decrease in the concentrations is noticed from 1989 to 1992 (Table 2). The congeners CB-52 (2,2′,5,5′-TeCB) and CB-101 (2,2′,4,5,5′-PeCB) occurred at low levels and corresponding CB methylsulphonyl metabolites ($MeSO_2$-CBs) were also found in the milk (Norén *et al.* 1996). Parent compounds of the other $MeSO_2$-CBs were not found in the milk (Norén *et al.* 1996). CB-122 (2′,3,3′,4,5-PeCB) could not be confirmed by GC-MS analysis. The rate of the decline in concentrations of coplanar CBs (Table 1) was different for the congeners and no manifest decrease in the concentration of CB-169 (3,3′,4,4′,5,5′-HxCB) was seen from 1972 to 1992. This may be explained by the structure of this congener, *i.e.* the high degree of chlorination and the lack of two adjacent unsubstituted positions close to chlorine atoms predicts a highly stable congener (Kimbrough 1980).

The levels of *p,p′*-DDT and *p,p′*-DDE in Swedish breast milk have decreased considerably since the first investigations in 1967 (1,270 and 2,040 ng/g fat, respectively) (Norén 1983b). The rapid decline of these compounds (Table 2) has led to changes in the ratios of organochlorine contaminants in the milk as shown for 1972 and 1992 (Figure 3). In all time periods *p,p′*-DDE (2,300–230 ng/g lipids) was the major chlorinated contaminant and its methylsulphonyl metabolite ($MeSO_2$-DDE) (5–0.4 ng/g lipids) the major aryl methyl sulphone compound (Norén *et al.* 1996).

There are no great differences in the levels of *p,p′*-DDT, *p,p′*-DDE, and total PCBs in breast milk from different parts of Sweden (Norén 1983a; Vaz *et al.* 1993). In a Norwegian study of milk sampled in 1991 from 28 mothers living in Oslo (Johansen *et al.* 1994), the concentrations of DDT compounds and different congeners of CBs were similar to those in milk sampled in the same year in Stockholm. However, the levels of non-*ortho*-substituted coplanar CB congeners were higher than in milk from Stockholm; the highest concentration was noticed for CB-169, not for CB-126 as in milk from Stockholm. The levels in milk from other parts of Norway were similar to those in Stockholm (Becher *et al.* 1995). Also the levels of DDE, HCB, and PCBs reported from Denmark were similar for the corresponding years from Stockholm (Hilbert *et al.* 1996). In a Canadian investigation of 497 human milk samples from 1992 (Newsome *et al.* 1995), the levels were similar to our results of *p,p′*-DDE, *p,p′*-DDT, and *o,p′*-DDT, but differed for PCBs and HCB, which were about two times higher in Swedish milk (Table 2).

The concentrations of PCDD and PCDF expressed as TEQs in the milk from Stockholm, 15 pg TEQs/g fat in 1984–85 (Table 4) were equal to the reported levels from Norway and Denmark for samples collected in the same period (Clench-Aas *et al.* 1992; Hilbert *et al.* 1996). However, slightly higher levels have been reported in milk from highly industrialized areas in Sweden (Clench-Aas *et al.* 1992). From 1984–85 to 1992 only minor changes in TEQs are discerned (Table 4). As previously noted (Norén and Lundén 1991; Johansen *et al.* 1994), the contribution of non-*ortho*- and mono-*ortho*-substituted CB congeners to the dioxin-related toxicity has to be considered in human risk assessment (Figure 4). In *in vitro* enzyme induction assays, the HxCNs and HpCN were at least as active as certain coplanar CBs (Hanberg *et al.* 1990), but their contribution to the sum of TEQs (0.5–1.0%) in the milk was of minor importance (Figure 4, Table 4).

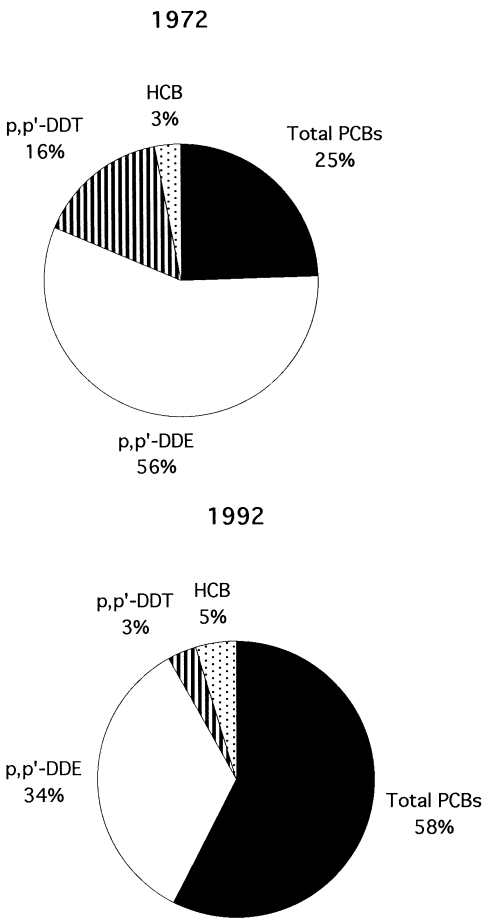

Fig. 3. Distribution of organochlorine compounds in Swedish breast milk. The total levels were 4,414 ng/g fat in 1972 and 661 ng/g fat in 1992. Sum of PCNs, sum of PCDDs, and sum of PCDFs were $< 0.1\%$, respectively

Although it cannot be excluded that infants may be more sensitive than adults to these organochlorine contaminants, the WHO expert group has concluded that the margin between intake and levels that may cause health effects is secure for breast-feeding and the positive impact of breast-feeding should be promoted (Grandjean *et al.* 1988). The decrease in the TEQ levels in breast milk from 1972 onward is a clear improvement with positive effects on diminishing an infant's pre- and postnatal exposure to these contaminants. However, considering the fact that the decrease from 1985 to 1992 is small and the recent findings that certain organochlorine compounds may interfere with endocrine and neurological systems, additional knowledge about exposure and toxic effects is still needed.

Conclusions

Swedish breast milk evidently was considerably contaminated with different chlorinated compounds in the early 1970s. In addition to the presently reported PCBs, PCNs, PCDDs,

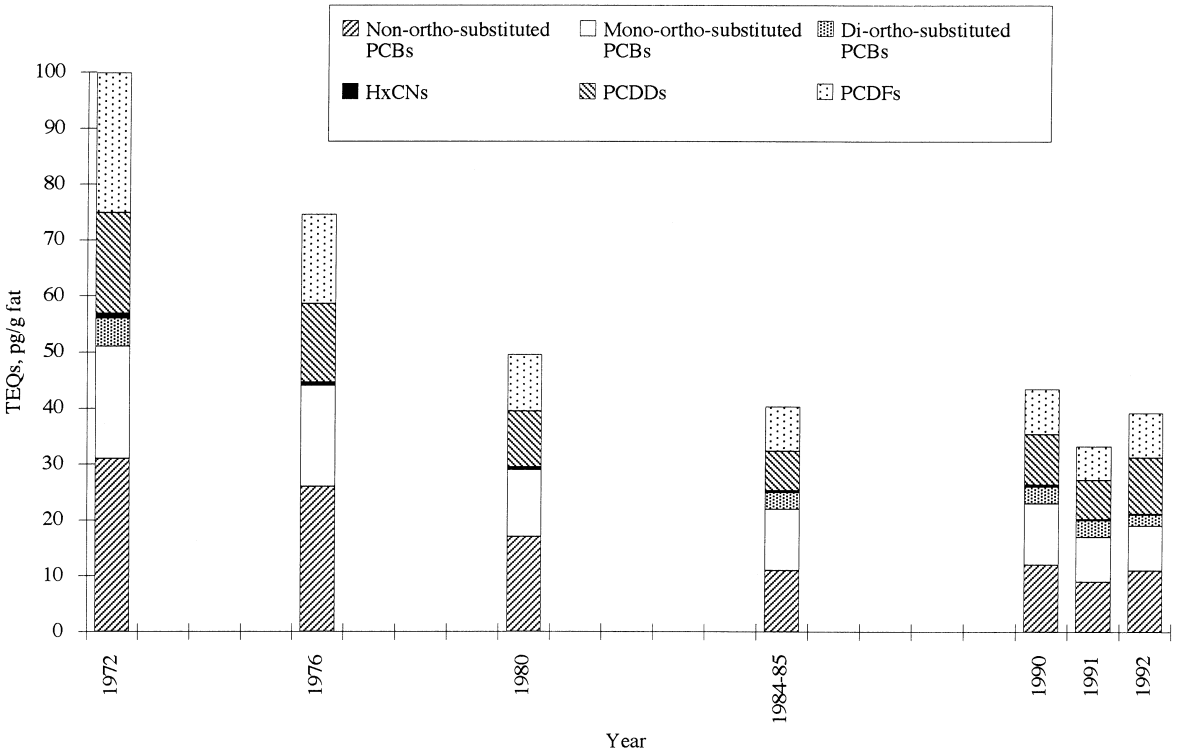

Fig. 4. Contribution of toxic equivalents (TEQs) from PCBs, PCNs, PCDDs, and PCDFs, expressed as pg/g fat, in Swedish human milk

PCDFs, DDT, DDE, and HCB, several organochlorine pesticides, *e.g.* dieldrin, isomers of hexachlorocyclohexane and chlordane compounds, have been found in human milk (Norén 1983a,b, 1988). The occurrence of PCN in milk has not been previously reported and may have reached higher levels together with other contaminants before the sampling of milk was started. Fortunately, there is a decline in the levels of almost all compounds during the two decades studied. However, the rate of decline differs for the individual compounds. The most pronounced decline is seen of *p,p′*-DDT, while the decline of CB-169, for example, is negligible.

Investigations including a great number of related organochlorine compounds give more complete information about the contamination of breast milk and, accordingly, the exposure of mothers and their infants. Multicomponent investigations provide information considering the total input of related toxic compounds in estimation of harmful effects to an infant. In this respect the metabolites of the compounds also have to be considered.

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