

Final report to The Michigan Great Lakes Protection Fund

Exposure to polybrominated diphenyl ethers (PBDE) and hydroxylated polychlorinated biphenyls (HO-PCB) in breast milk samples from Michigan fish eaters and in fish samples

by

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December 1, 2007

Summary

The **specific objectives** were:

1. Determine the exposure of PBDE and HO-PCB in human breast milk sample with and without fish consumption to facilitate comparison with data from other regions.
2. Determine the concentrations of halogenated organic compounds (HOC) in fish samples, including different fish species, from places where the participants caught their fish. This will allow comparison with data from other regions.
3. Assess by means of linear regression analyses whether consumption of Great Lakes fish, and the burden of the consumed fish, can significantly explain the variance of PBDE and HO-PCB concentrations in human breast milk samples. In these analyses, we will control for other sources of HOC exposure such as meat consumption, milk, and occupational exposure.

The support by the Michigan Great Lakes Protection Fund started in January 2002. This investigation was added to the ongoing study 'Pregnancy, Environment, And Child Health' (PEACH), funded by the US Environmental Protection Agency. In addition, we had parallel funding from the Agency for Toxic Substances and Disease Registry (CDC) for a follow-up of

Part 2

The specific 2nd objective was:

Determine the concentrations of halogenated organic compounds (HOC) in fish samples, including different fish species, from places where the participants caught their fish. This will allow comparison with data from other regions.

Concentration of dichlorodiphenyl trichloroethane (DDT) and its metabolites dichlorodiphenyl dichloroethane (DDD) and dichlorodiphenyl dichloroethylene (DDE) and of Polychlorinated Biphenyls (Aroclor) in Michigan Sport Caught Fish

Abstract

Exposure to halogenated compounds (HOC) from eating sport caught fish (SCF) has developed from simple classifications as exposed/unexposed to consideration of frequency of consumption, year, and fish species. However, little is known to what extent conventional indicators such as year and fish species and additional characteristics such as location determine fish tissue concentration (FTC) and thus available dose to humans. Using the Michigan Department of Environmental Quality FTC monitoring dataset containing 3,876 fish tissue specimens collected from Lake Michigan and Lake Huron between 1983-2004, we estimated potential PCB exposure using a multivariate linear regression of log FTC-HOC modeled on species, location, specimen fat, and collection year. The model explains 85% of the variance of sum of the concentration of dichlorodiphenyl trichloroethane (DDT), dichlorodiphenyl dichloroethane (DDD), and p,p'-dichlorodiphenyl dichloroethylene (DDE) in fish tissue and 70% of the variance of total PCB (Aroclor). Controlling for fat content, fish species contributed 49 and 42% (DDT/DDD/DDE and total PCB respectively). Sampling location explained a variance of 17% for DDT/DDD/DDE and 13.6% for PCB. Calendar year contributed 11% and 7.4%, respectively.

We conclude that for this dataset, species and location provide important information and should be included when estimating the intake of HOC from sport-caught fish.

Introduction

Eating Great Lakes sport caught fish (SCF) is considered a significant route of human exposure to halogenated compounds (HOC) such as dichlorodiphenyl trichloroethane (DDT), its metabolites p,p'-dichlorodiphenyl dichloroethylene (DDE) and, dichlorodiphenyl dichloroethane (DDD), and polychlorinated biphenyls (PCBs) in the Great Lakes Basin¹⁻⁴. Among anglers choosing to eat their catch, several studies have reported a relationship between eating Great Lakes SCF fish and human PCB levels⁵⁻¹⁷. In 1991, the state of Michigan had a total of 1.7 million sport fish anglers who spent 24.5 million days fishing¹⁸. Thus, anglers represent a large population at risk of exposure to HOC from this route.

DDE and DDE are metabolites of dichlorodiphenyltrichloroethane (DDT), which had widespread use from the 1940s to the 1960s. Both DDT and DDE are lipophilic and bioaccumulate in the food web. The long biologic half-life of DDE accounts for its ubiquitous presence in human populations.^{19,20} The use of DDT was banned in the United States during the early 1970s. In the Great Lakes Basin, environmental influx of PCBs began in 1929 and continued until being banned in 1977. PCBs were valued for their highly inert properties and were used extensively in industrial applications²¹. Because of their inert characteristics, PCBs released into the environment are highly persistent.

In the United States, subsequent to being banned PCB concentrations in fish have declined substantially²²⁻²⁵. However, since the mid-1980's changes in PCB concentration in the Lake Michigan fish have been minimal²⁴. This is attributed to redistribution of PCBs trapped in sediments and airborne deposition. Over a long but unknown time span, environmental PCBs are expected to decline as they slowly degrade, are flushed out of water basins, dispersed by the atmosphere, or permanently buried in deep sediments. Because the available data are quite variable, it is difficult to discern whether concentrations in fish tissue are nearing a static equilibrium, decreasing slowly, or even increasing slightly^{24,26-28}.

Since HOC are highly lipophilic and tend to bioaccumulate in the lipids of humans, fish,

and other wildlife²⁹⁻³², their bioaccumulation in fish may be assessed as fish tissue concentration. The magnitude of bioaccumulation for a particular fish is determined by HOC in the water column, ecological factors, and species characteristics including fat content, longevity, and behavior³³.

Fish tissue fat content varies greatly from species to species and is positively correlated with PCB bioaccumulation³⁴. Smaller short lived forage fish tend to bioaccumulate less PCBs than long lived top predator fish. Carp and whitefish are bottom feeders, whereas ciscowet and walleye are predator fish occupying top levels of the food chain³⁵.

Regional ecological factors such as water body productivity and food chain structure modify HOC bioaccumulation rates³³. HOC bioaccumulation in fish tends to be inversely associated with water body productivity and the number of levels in the food chain. Lower FTC-HOC in fish from lakes of increasing productivity is attributed to higher fish growth rates and higher sedimentation of pollutant absorbing particles^{27,34,36-45}.

Michigan has a large and diverse fishery composed of the Great Lakes, rivers, streams, and inland lakes. Coincident with this diversity is a high potential for variation in factors that determine fish tissue concentration of total PCBs (FTC-HOC). This variation is evidenced by fish advisories from Michigan Department of Environmental Quality and Michigan Department of Community Health's Division of Environmental Health, Environmental Protection Agency (EPA) reports, and other literature, which report uneven geographical distributions of sediment, water column, and FTC-PCB⁴⁶⁻⁴⁹. Thus the potential ingested PCB and DDT/DDD/DDE dose from Michigan SCF is highly variable.

We conducted this analysis to determine which factors are important for prediction of FTC-HOC and to examine potential variation in FTC-HOC available dose in typical human exposure scenarios in the Great Lakes.

Methods

The data set used for statistical analysis consisted of State of Michigan, Department of Environmental Quality (DEQ) monitoring for FTC-HOC in 73 locations (Lake Michigan QNE Lake Huron) annually from 1983 to 2004. Sampling accrued 3,876 fish specimens.

Sampling

Sample site selection for fish sampling was based upon DEQ defined 'areas of concern' for PCB and DDT/DDD/DDE contamination. The data does not present a random sample of locations in the State of Michigan sports fishery. Also, because of limitations in sample availability, species sampled and numbers sampled are irregular from year to year.

Determination of Fish Tissue HOC Concentration

Monitoring data from collection years 1987 to 1997 are from analyses performed at the Michigan Department of Community Health, Health Risk Assessment Laboratory. Analytical procedures from the Health Risk Assessment Laboratory are documented in the Quality Assurance Manual for the Health Risk Assessment Laboratory (Michigan Department of Community Health, 1997). This manual also includes the laboratory's quality assurance and quality control processes. Before 1987, fish samples were analyzed at the Michigan Department of Natural Resources Laboratory. The samples were analyzed for total PCBs using the Webb-McCall packed column method with Aroclor 1254 as a quantitative reference standard⁵⁰. For the 1987 to 1997 data PCBs and pesticides were extracted using ethyl ether/petroleum ether 1:1 (v:v), and then separated using silica gel column chromatography. The fractions were analyzed on a packed column chromatograph equipped with an electron capture detector⁵⁰. The PCB congeners appear in fraction II, while the chlorinated pesticides are present in all four fractions.

Species and fat content

Samples include the 26 most commonly consumed species (Table 1). Since many species have limited ranges within the Michigan sports fishery, none of the sampling locations

have complete data for all species. A primary characteristic of different species is their fat content, which can be reduced during fish preparation. To separate species effects from fat contents, we statistically controlled for fat content, which was provided in the data set. In addition, we also considered weight and height. To take relative weight and height into account, we determined the maximum weight and height of the species and calculated the relative weight and height for each fish.

Location and calendar year

Samples were collected at 73 locations. Because of practical limitations to sample sizes and specimen availability, sampling was rarely complete for any one species across all time periods at a particular location. These sampling irregularities required some sampling locations to be aggregated in the analyses. In the analysis, aggregation units retain all names of component sampling locations (Table 2). Information was available for the period between 1983 and 2004 for DDT/DDD/DDE and from 1983 to 1999 for PCBs.

Statistical analysis

Data were analyzed using the generalized linear models procedure in SAS 9.1 software (SAS institute Inc. 2007). We used multivariable regression models to estimate the effect of species, sampling locations, calendar years, and fat contents on HOC in FTC. Based on univariate analysis, the HOCs were log-transformed to normalize the distributions. In linear regression analysis, we modeled for collection year, species, location, and percent fat content. Geometric means (GMs) were used for summarizing FTC-HOC levels because most distributions were skewed. To investigate for time trend in FTC-HOC we compare adjusted GMs by collection year group for all locations.

Results

On average, the median fish tissue concentration (FTC) of total PCBs was about 3 times higher than those of DDT and its metabolites DDD and DDE (0.78 ppm vs. 0.23 ppm). Both halogenated organic compounds were correlated ($r_{\text{Spearman}}: 0.86215, n=3589, p<.0001$). An analysis of the ratio of the concentration of PCB to DDT and metabolites shows that fat content is the common predictor. However, location, species, and calendar year significantly affect the ratio (data not shown). Although highly correlated, PCBs and DDT and its metabolites thus vary independently with location, species, and calendar year and cannot substitute for one another.

The regression model of total PCBs on collection year, location, species, and species adjusted weight explained approximately 85% of the variance of the concentration of DDT and its metabolites DDD and DDE in fish tissue, and 70% of the variance of FTC-PCB (Table 1). Regarding DDT/DDD/DDE, fish species contributed 49%, sampling location contributed 17%, collection year contributed 11%, and specimen fat content contributed 8.2%. For total PCB, species contributed 41.7%, sampling location contributed 13.6%, collection year contributed 7.4%, and specimen fat content contributed 6.9%. As additional confounders, we considered weight and length of the fish sample. Both were correlated ($R_{\text{Spearman}}: 0.97, p<0.0001$). The addition of relative weight nor relative height did add to the explained variance of DDT/DDD/DDE in fish tissue nor FTC-PCB.

Species-specific geometric means (GM) adjusted for collection year, location sampled and specimen fat content generated statistically different values (Table 1). The general trend is for higher concentrations in species that are long lived, fatty fleshed, top predators, or bottom dwellers. Five species have the highest values for both DDT/DDD/DDE and PCBs. These are carp, channel catfish, lake sturgeon, lake trout, and longnose sucker. For exposure assessment of a typical Michigan angler study population, it is important to take into consideration commonly eaten species. Comparing two such species reveals that lake trout has about a 10-fold higher adjusted FTC-HOC than yellow perch (Table 1).

Statewide variation in location-specific adjusted GMs for FTC-HOC is related to water body proximity to industrialized areas. FTC-PCBs are highest in developed areas of Southern Michigan and decrease towards Northern Michigan (Table 2). The lowest adjusted GM FTC-PCB is seen in fish from the Thunder Bay.

In the 1983 to 2004 monitoring window, we observed significantly lower levels in 2003 and 2004 for the sum of DDE, DDD, DDT and in 1998 and 1999 for PCBs (Table 3). When treating calendar time as linear variable, there is a statistically significant reduction in the sum of DDE, DDD, and DDT of 1% per year between 1983 and 2004 and a reduction of PCB of 1% per year between 1983 and 1999. In addition, this trend is not consistent in specific locations. The models for the sum of DDE, DDD, and DDT and for PCBs showed statistically significant interaction between location and time. For instance, the sum of DDE, DDE, and DDT in fish from the St. Joseph River at Berrien Springs (n=302) show no discernable time trend for decline.

Our analyses included data for fish from several trophic levels, including the forage species alewife and spottail shiners. When excluding alewife and spottail shiners, the explained variance of the regression model for the sum of DDE, DDD, and DDT was reduced to 80%; there was no reduction for PCBs. The exclusion did not substantially change the adjusted geometric mean (less than 5% of the original value).

Discussion

We found that variance of fish tissue concentration of total HOC was best explained by species (variance explained: 49% for the sum of DDE, DDD, and DDT and 41.7% for PCBs) and location (17 and 13.6%, for the sum of DDE, DDD, and DDT and for PCBs, respectively). Calendar year, although statistically significant, did contribute the least to the variance (11 and 7.4%, respectively). This analysis leads us to infer that location may be a significant factor in assessing human exposure to PCBs from eating sport caught fish in Michigan waters. A fish-PCB index limited to species, frequency, and duration may thus be an inappropriate proxy

variable for exposure. In addition, because of ecological variability in water body productivity and food web structure, there is possibly that location and species are associated ⁵¹.

Because this data set is not a random sample of the State of Michigan sports fishery, it is important to consider its limited generalizability to the entire Michigan sports fishery ⁵¹. Additionally, not all locations had complete information for all species and years. The nonrandom sampling by location across collection year may bias estimates of time trends in FTC-HOC. Another potential bias may originate from changes in average specimen fat content across calendar year, although we did not identify any trend for change in average specimen fat across calendar year group.

Variations in contaminant levels between locations are consistent with existing publications of differences in PCB contamination by location ⁵². Newsome and Andrews found PCB tissue concentrations among Carp samples to be among the lowest in commercial fisheries samples and among the highest in contaminated areas ⁵³. The United States Environmental Protection Agency (EPA) and Michigan DEQ identified 'areas of concern' for PCB contamination correlate with FTC-PCB from our analysis ³. However, the implications of these location differences have not been integrated into individual exposure assessment.

In the US, there are subpopulations of regular fish consumers who seem to be at higher risk for exposure to PCB because of their proximity to polluted water bodies ⁵⁴. Concern about subpopulations that represent minorities is a special issue for environmental justice. Of these subpopulations, many are unaware of, or do not heed fish consumption advisories. An extensive survey of people who live in the Great Lakes states found that less than 50 percent of those who ate fish from the Great Lakes were knowledge of the advisories ⁵⁵.

Many reports of time trends in FTC-HOC in Michigan waters show reductions in levels ⁵⁶. Other publications suggest that FTC-HOC concentrations have remained fairly constant since the early 1980's ⁵⁷. Based on our multivariate analysis of the DEQ monitoring data, we observed a linear weak reduction of about 1% per year. The Great Lakes Strategy 2002

established the long-term goal that lake trout PCB should decline 25% from 2000 to 2007.⁵⁸ For PCB in lake trout we also find a reduction of approximately 1% per year. Hence, given these findings, a maximum reduction of 7% could be expected between 2000 and 2007. In addition, determination of PCB in our data ended in 1999.

Conclusion

Our analysis is consistent with observations of the importance of species as a factor in determining available of PCB and the sum of DDT and its metabolites DDE and DDD for Michigan sport fish eaters. Additionally we conclude that in Michigan waters, water-body and location from which sport fish are caught are important factors in valid prediction of the likely intake. Since 1983, there is only a small reduction of HOC in fish samples, thus the Great Lakes Strategy 2002 is likely to be achieving its goal.

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Table 1: Geometric mean of fish tissue concentration for the sum of DDE, DDD, and DDT and of total PCBs (ppm) adjusted for collection year, location sampled, and specimen fat concentration for the sampling period of 1983-2004 (DDE, DDD, DDT) or 1983-1999 (PCB)

	Sum of 4,4-DDE, 4,4-DDD, and 4,4'DDT (ppm)			Total PCB - Aroclor (ppm)		
	n	Geometric mean		n	Geometric mean	
Alewife	154	0.134	**	4	0.323	**
Brown Trout	169	0.211	**	180	0.662	**
Burbot	23	0.041	**	13	0.149	
Carp	198	0.361	**	220	1.299	**
Channel Catfish	113	0.287	**	146	0.976	**
Chinook	680	0.263	**	759	1.111	**
Chub	34	0.133	**	34	0.425	**
Coho	628	0.132	**	646	0.499	**
Lake Sturgeon	18	0.707	**	10	2.092	**
Lake Trout	387	0.329	**	367	0.773	**
Lake Whitefish	190	0.176	**	190	0.335	**
Longnose Sucker	22	0.474	**	22	1.275	**
Northern Pike	15	0.059	**	15	0.146	**
Rainbow Smelt	162	0.111	**	162	0.370	**
Rainbow Trout	106	0.122	**	105	0.335	**
Redhorse Sucker	10	0.110	**	-	-	
Rock Bass	4	0.010	**	-	-	
Round Goby	84	0.013	**	-	-	
Smallmouth Bass	16	0.042	**	7	0.381	
Splake	7	0.178	**	7	0.499	**
Spottail Shiner	150	0.090	**	-	-	
Walleye	197	0.093	**	189	0.325	**
White Bass	21	0.237	**	11	1.415	**
White Perch	8	0.067	**	8	0.362	**
White Sucker	60	0.062	**	50	0.227	**
Yellow Perch	133	0.032	(Ref)	133	0.084	(Ref)
Explained variance by the model (R ²)		85.1%			70.1%	

Ref Reference for the assessment of statistical differences.

** p ≤ 0.01

The five highest values are highlighted.

Table 2: Geometric mean of fish tissue concentration collected at different locations for the sum of DDE, DDD, and DDT and of total PCBs (ppm) adjusted for collection year, species, and specimen fat concentration for the sampling period of 1983-2004 (DDE, DDD, DDT) or 1983-1999 (PCB)

Location	Sum of 4,4-DDE, 4,4-DDD, and 4,4-DDT (ppm)			Total PCB - Aroclor (ppm)		
	n	Geometric mean		n	Geometric mean	
Alpena	4	0.127		4	0.689	**
Au Sable River	104	0.113	*	119	0.372	
Big Bay De Noc	10	0.076		10	0.365	
Black River	38	0.124	**	38	0.317	
Bridgeman	2	0.027	*	-	-	
Charlevoix	20	0.094		24	0.248	
Charlevoix/Little Traverse Bay	10	0.074		10	0.295	
East of Bois Blanc Island	6	0.204	**	6	0.395	
Epoufette	6	0.041	*↓	6	0.109	**
Glen Haven	10	0.185	**	10	0.588	**
Grand Haven	40	0.202	**	49	0.800	**
Grand River, Grand Rapids	25	0.204	**	25	0.644	**
Grand River, Webber Dam	195	0.192	**	195	0.554	**
Grand Traverse Bay	50	0.146	**	50	0.588	**
Grand Traverse Bay, East Arm	32	0.220	**	32	0.451	*
Grand Traverse Bay, West Arm	32	0.151	**	32	0.462	*
Green Bay	38	0.128	**	26	1.429	**
Green Bay, Cedar River	57	0.115	**	47	0.444	*
Grindstone City	40	0.060		30	0.313	
Hammond Bay	12	0.235	**	12	0.485	*
Harbor Beach	10	0.132	*	10	0.706	**
Kalamazoo River mouth	2	0.025		-	-	
Leland	3	0.223	**	3	0.581	
Lexington	2	0.120		2	0.550	
Little Bay De Noc	149	0.129	**	107	0.558	**
Little Manistee River Weir	25	0.144	**	44	0.538	**
Little Traverse Bay	16	0.099		16	0.518	*
Ludington	21	0.122	*	20	0.392	
Manistee	4	0.282	**	4	0.483	
Manistee Lake	1	0.109		-	-	
Manistee River	92	0.198	**	99	0.487	*
Manitou Islands	4	0.293	**	4	0.699	*
Marquette Island	6	0.187	**	6	0.890	**
Menominee River	10	0.224	**	10	1.446	**
Millecoquins River	1	0.054		-	-	
Muskegon	37	0.120	**	37	0.472	*
New Buffalo	1	0.054		-	-	
Northern Lake Michigan	20	0.084		10	0.569	
Norwood	6	0.139	*	6	0.463	
Nunns Creek	10	0.068		10	0.140	**↓

Oscoda	6	0.094		6	0.408	
Pentwater	43	0.132	**	43	0.433	*
Platte River	290	0.203	**	305	0.584	**
Platte River Hatchery	15	0.334	**	15	0.877	**
Point Betsie	9	0.115		9	0.430	
Port Austin	39	0.100		40	0.391	
Port Sanilac	10	0.125	*	10	0.551	*
Rock Falls Creek	10	0.157	**	10	0.723	**
Rockport	40	0.075		40	0.283	
Saginaw Bay	300	0.020	**↓	8	-	
Saginaw Bay, Au Gres	86	0.072		86	0.402	
Saginaw Bay, Bay Port	105	0.059		46	0.392	
Saginaw Bay, Caseville	6	0.075		20	0.493	*
Saginaw Bay, Charity Island	10	0.083		10	0.419	
Saginaw Bay, Fish Point	50	0.094		50	0.611	**
Saginaw Bay, Pinconning	8	0.025	**↓	8	0.051	**
Saginaw Bay, Rifle River	20	0.095		20	0.694	**
Saginaw Bay, Sand point	6	◆		7	◆	
Saginaw Bay, Sebewaing	1	0.418	**	1	2.394	**
Saginaw Bay, Wildfowl Bay	38	0.063		129	0.309	
Saginaw Bay, near Saginaw River mouth	161	0.077		162	0.478	**
Saginaw Bay, off Saginaw River	36	0.086		36	0.548	**
South Fox Island	7	0.254	**	7	0.659	**
South Haven	232	0.104	*	174	0.444	*
South Point	14	0.075		14	0.332	
Southern	58	0.108	*	58	0.387	
St. Joseph River, Berrien Springs	302	0.199	**	297	0.586	**
Sturgeon Bay	2	0.121		2	0.492	
Swan River	132	0.133	**	152	0.443	*
Tawas Bay	4	0.167	*	4	0.560	
Tawas River	60	0.188	**	70	0.523	**
Thompson Creek	166	0.143	**	166	0.510	**
Thunder Bay	152	0.091		142	0.378	
Thunder Bay River	20	0.073	(Ref)	20	0.302	(Ref)

Ref Reference for the assessment of statistical differences.

* $p \leq 0.05$, ** $p \leq 0.01$

◆ The adjusted mean cannot be estimated, since only Walleye were caught.

For the sum of DDE/DDD/DDT values above 0.2 ppm, for total PCB, value above 0.55 are highlighted.

Table 3: Geometric means of fish tissue concentration of the sum of DDE, DDD, and DDT and of total PCBs (ppm) adjusted for location sampled, species, and specimen fat concentration for the sampling period of 1983-2004 (DDE, DDD, DDT) or 1983-1999 (PCB)

Year	Sum of 4,4-DDE, 4,4-DDD, and 4,4'DDT (ppm)			Total PCB - Aroclor (ppm)		
	n	Geometric mean	**	n	Geometric mean	**
1983	242	0.110	**	243	0.463	**
1984	243	0.111	**	243	0.421	**
1985	151	0.126	**	246	0.628	**
1986	153	0.108	**	286	0.728	**
1987	276	0.168	**	275	0.666	**
1988	145	0.142	**	186	0.525	**
1989	207	0.143	**	207	0.476	**
1990	158	0.128	**	158	0.468	**
1991	239	0.122	**	239	0.484	**
1992	143	0.147	**	143	0.492	**
1993	232	0.142	**	232	0.425	**
1994	138	0.181	**	138	0.634	**
1995	79	0.115	**	79	0.387	
1996	141	0.109	**	141	0.482	**
1997	142	0.129	**	142	0.458	**
1998	281	0.123	**	281	0.267	
1999	46	0.081		45	0.298	(Ref)
2000	11	0.055	**		-	
2001	25	0.096	**		-	
2002	6	0.117	**		-	
2003	307	0.099	(Ref)		-	
2004	224	0.045			-	

Ref Reference for the assessment of statistical differences.

** $p \leq 0.01$

Figure 1: Adjusted geometric mean of the sum of DDT and its metabolites DDE and DDE in fish tissue by Collection Year (adjusted for fish species, location, and fat content)

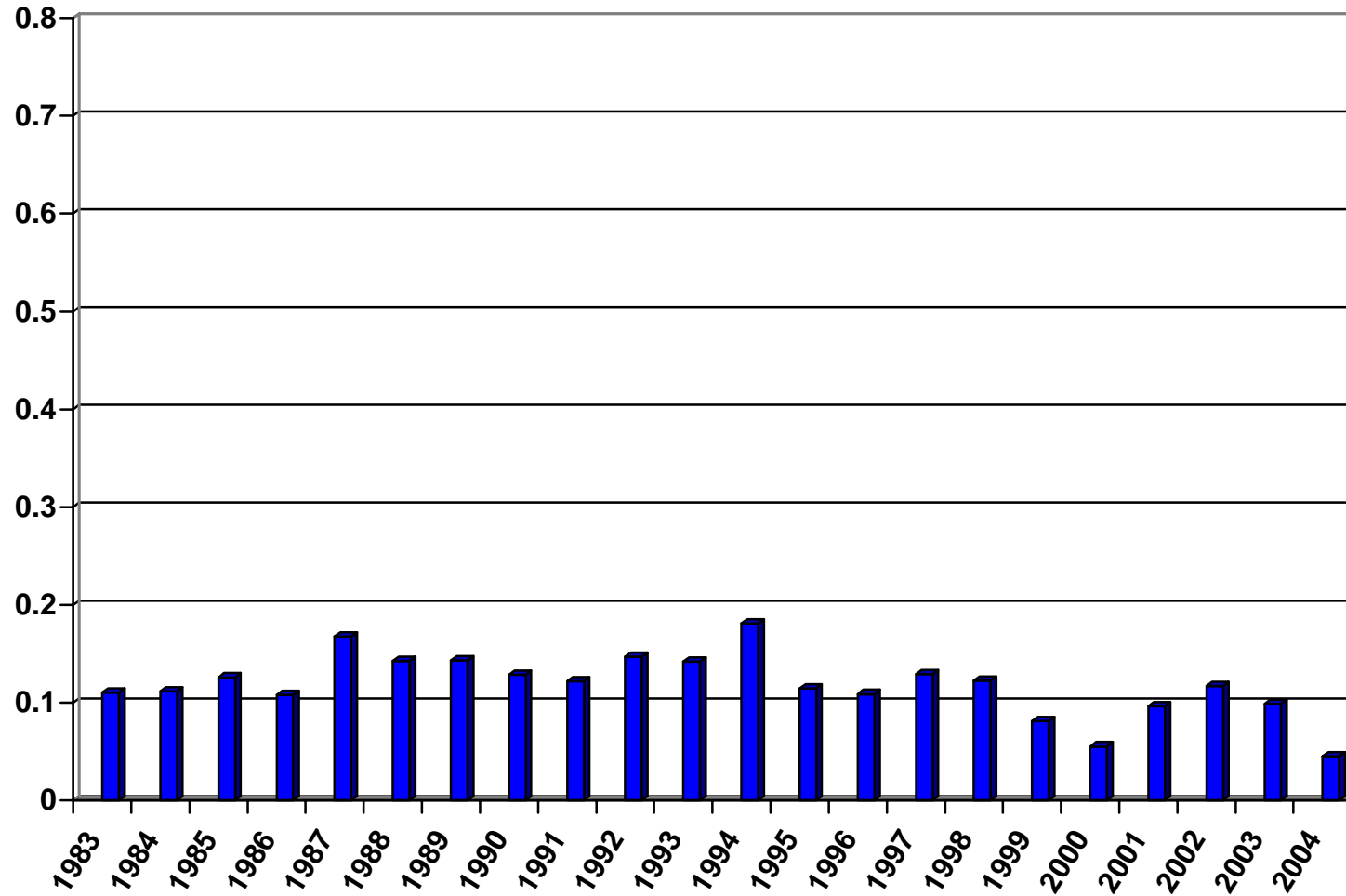
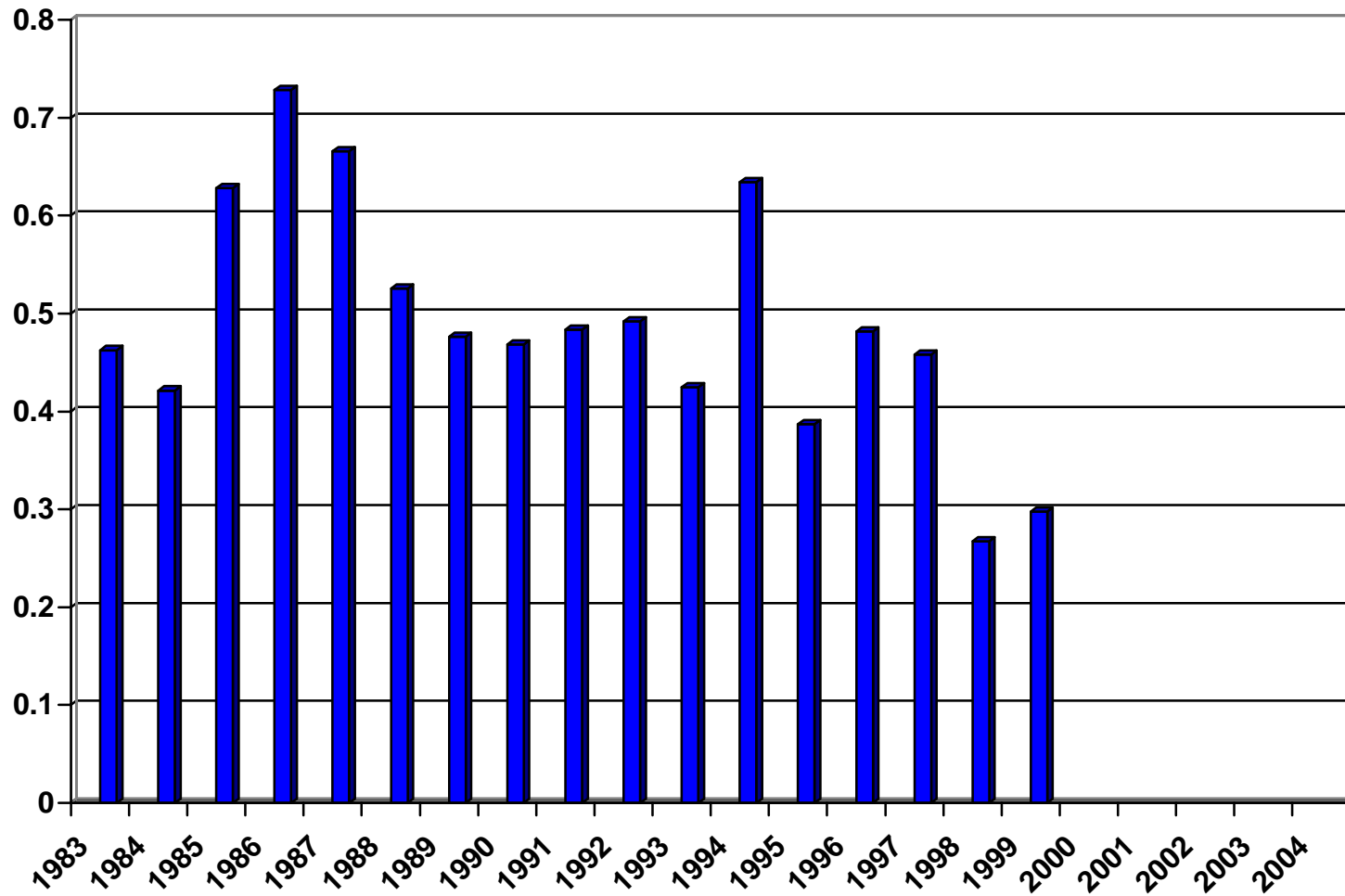


Figure 2: Adjusted geometric mean of total PCBs (Aroclor) in fish tissue by Collection Year (adjusted for fish species, location, and fat content)



Part 1 and 3

The specific 1st and 3rd objectives were:

1. Determine the exposure of PBDE and HO-PCB in human breast milk sample with and without fish consumption to facilitate comparison with data from other regions.
3. Assess by means of linear regression analyses whether consumption of Great Lakes fish, and the burden of the consumed fish, can significantly explain the variance of PBDE and HO-PCB concentrations in human breast milk samples. In these analyses, we will control for other sources of HOC exposure such as meat consumption, milk, and occupational exposure.

Introduction

Infants of mothers exposed to halogenated organic compounds (HOC) such as polychlorinated biphenyls (PCBs) and p,p'-dichlorodiphenyl dichloroethylene (DDE) have higher concentrations of PCBs and DDEs as a result of both *in utero* and breastfeeding exposure. It is estimated that approximately 10-12% of total lifetime exposure can occur via nursing.¹ A nursing infant may receive as much as 50 times the daily exposure of an adult.²⁻⁴ Breast milk is unique as a matrix for biomonitoring as it also serves as a food source for a segment of the human population.⁵ In addition, breast milk monitoring is a convenient noninvasive means of collecting relatively large volumes (50-100 ml) of specimen to estimate the chemical burden of the mother as well as for the breastfed child. Data on HOC concentrations in breast milk in the US are limited and the findings on trends are inconsistent. PCB concentrations in human milk are likely to have declined in Michigan anglers since the last determination, published in 1983.⁶ In Sweden, an exponential increase in polybrominated diphenyl ethers (PBDE) in breast milk was identified: the sum of PBDE in human milk in Sweden increased from 0.07 ng/g lipids to 4.02 ng/g lipids from 1972 to 1997.⁷ The finding raised concern about potential and comparable exposures in the Great Lakes region. Additionally, new reports emphasized the potential adverse health impacts from PBDE.^{8,9}

Halogenated organic compounds (HOC) of interest include polybrominated diphenyl ethers (PBDE), polychlorinated biphenyls (PCB), polybrominated biphenyls (PBB), and dichlorodiphenyl dichloroethene (DDE), a metabolite of dichlorodiphenyl trichloroethane (DDT). It has been demonstrated that PCB and DDE in fish contribute to higher PCB and DDE concentrations in the breast milk of fish eaters.^{6,10-14} In addition to PCB and DDE, this study focused on polybrominated diphenyl ethers (PBDE), a newly emerging HOC. Time trends for PBDE levels in the environment differ from those of PCB and DDE: PBDE levels increase or remain constant, whereas the levels of most other persistent compounds decrease.¹⁵

DDE and DDE are metabolites of dichlorodiphenyltrichloroethane (DDT), which had

widespread use as a pesticide from the 1940s to the 1960s. Both DDT and DDE are lipophilic and bioaccumulate in the food web. The long biologic half-life of DDE accounts for its ubiquitous presence in human populations.^{16,17} The use of DDT was banned in the United States during the early 1970s.

PBBs are brominated hydrocarbons, with a structure related to other chemical compounds such as PCBs, dioxins, and furans. One of their most important physical properties is that they have a high flammability point, and for this reason they have been used as flame retardants. PBBs are lipophilic with a long half-life (around 11 years) in animals and humans and the potential for biomagnification.¹⁸ In the summer of 1973, a fire retardant product (FireMaster FF-1[®]), containing PBBs, was mistakenly added to animal feed and distributed to farms throughout Michigan. As a result, approximately 295 kg of PBBs entered the food web.¹⁹ It can still be identified in West-Michigan populations.

Environmental influx of PCBs began in 1929 and continued until being banned in 1977. PCBs were valued for their highly inert properties and were used extensively in industrial applications²⁰. Because of their inert characteristics, PCBs released into the environment are highly persistent.

Polybrominated diphenyl ethers (PBDE) are one class of flame retardant, which were added to polymers used in electronic equipment (computers, TV sets), construction material, coatings and textiles. Waste from these products is probably the main source of PBDE (municipal waste, landfills, incineration). PBDE seems also be released into the environment through sewage and from volatilization from electrical products.¹⁵ PBDEs were first identified in sediments in the United States and in fish from Sweden.^{21,22} The occurrence of PBDE is due to anthropogenic sources. Air deposition from local and global sources seem to be the most important route of exposure of lakes.²³ PBDEs have also been found in human blood and milk.¹⁵ According to a Swedish study, major isomers in human milk are BDE-17, BDE-28, Bde-47, BDE-99, BDE-100, BDE-153, and BDE-154.⁷ In the 1990s, the concentration of the sums of PBDE congeners in

human milk were, on a lipid-base, similar to those reported in blood.^{24,25} For the general population, consumption of contaminated fish is considered an important source of exposure to PBDE.⁷ However, occupation (e.g. recycling of electronics) may also be a source of human exposure.²⁶ The half-life of PBDE seems to be in the range of 4-17 years,²⁷ however data are sparse and contradictory.^{15,28}

This study will compare PCB, PBB, DDE, and PBDE concentrations in human milk to determine whether one single HOC, for instance PCB, can serve as a marker for others, or whether HOC concentration are not correlated, indicating that they have different paths of exposure, different time-lines of exposure, or different kinetics and distributions in various body compartments.

Halogenated organic compounds (HOC) bioaccumulate in maternal fat over a woman's life span and result in maternal fat stores containing a higher concentration of HOC than from her daily dietary fat intake. In the case of only occasional HOC exposure, the increase in fat will be a mixture of mobilized maternal and dietary fat. In a review, DeKoning et al. showed that the relation of maternal serum to breast milk concentration varied widely.²⁹ Recently, Jaraczewska *et al.* reported that PCB and DDE in maternal serum and breast milk are only moderately correlated (Spearman's rank correlation coefficient $<.5$).³⁰ However, PCB and DDE were highly correlated comparing maternal serum and cord serum (Spearman's rank correlation coefficient $>.75$). While some studies collected HOC from cord serum,³¹⁻³⁶ other used placental tissue concentrations.³⁷⁻⁴¹ It is reasonable to assume that placental and cord serum concentration provide identical information on prenatal exposures.

The extent to which HOC in human milk, in maternal serum, and in placental tissues can substitute one another is not sufficiently known. In addition, it is in dispute whether the highest HOC exposure for the newborn occurs during pregnancy or via breast milk. Hence, this study will compare maternal HOC concentrations in serum, placental tissues, and breast milk.

Several past studies have shown that fish consumption is associated with increased PCB

and DDE concentration in women.^{6,7,42,43} In a sample of 12 primiparous nursing women from Japan, a strong correlation between PBDE concentration in human milk and dietary intake of fish and shellfish was established.⁴⁴ However, Danderud et al. in 39 primiparous women from Sweden, could not identify a correlation between fish consumption and breast milk PBDE levels.⁴⁵ Hence, this Michigan study will assess whether HOC concentration in maternal serum, placental tissues, and breast milk are related to fish consumption. In addition, we will compare serum concentrations in pregnant women with data collected in female offspring of the Michigan fishheater cohort.

Methods

Mother-infant samples

Primiparous women in their first trimester were enrolled in the Michigan part (Benton Harbor, St. Joseph, and Flint) of the Pregnancy, Environment and Child Health (PEACH) study. Ethical approval was granted by the Michigan State University Committee on Research Involving Human Subjects. Telephone interviews were conducted to collect information on maternal life style. Pregnancy and delivery information were abstracted from medical records. Maternal serum was collected around week 20 of the pregnancy. A placental sample was taken after delivery when the cord was disconnected from the placenta. Breast milk samples were collected in the first month post-partum.

Samples from female offspring of Michigan fish eaters

The Michigan fishheater cohort and the female offspring study group have been described elsewhere.⁴⁶⁻⁴⁹ Briefly, female offspring were re-contacted in 2006-2007 and blood sample was collected to determine HOCs.

Determination of PCB, PBB, PBDE, and DDE

The Analytical Chemistry Section Laboratory (ACSL) at the Michigan Department of Community Health performed the laboratory analysis for PCB congeners, PBB, and DDE. In brief, organochlorine compounds (OC) were extracted into diethyl ether-hexane (1:1 v/v). The extract was passed over a Florisil column. The 6% (v/v) diethyl ether in hexane fraction from the Florisil column was further fractionated into a PCB fraction and a pesticide fraction using a fully activated silica gel 60 column. PCB and DDE analysis were performed by high-resolution gas chromatography with electron capture detection (ECD) according to the modifications of the procedure reported by Najam et al. and Mullin et al.^{50,51} The PBBs and other organochlorine pesticides were analyzed using the modifications of a procedure by Needham et al.⁵². ACSL investigated 37 different PCB congeners (with a limit of detection of 0.03µg/L for the highest and 0.125 µg/L for the lowest ECD responding PCB congeners). Nine PBDE congeners were determined (PBDE028, 047, 077, 100, 099, 085, 154, 153, 183). The detection limit for PBDE was 0.13µg/L, 0.063 µg/L for PBB153, and 0.125 µg/L for p,p'-DDE. The total PCB concentration was calculated as the sum of the reportable PCB congeners at or above the respective limit of detection (LOD). The lipid content in serum, placental, and breast milk samples were determined with gravimetric methods. The HOC concentration is provided on a lipid base (ng/g lipid).

Statistical analyses

Regarding values below the limit of detection (LOD), we used two approaches, we imputed ½ of the detection limit for all observations below the LOD^{53,54}. For descriptive purposes, medians along with their corresponding 5th and 95th percentiles are provided. To compare HOC levels in the different matrices, Spearman rank correlations were computed. All analyses were conducted using SAS version 9.1⁵⁵.

Results

Data on 45 pregnant women with at least one HOC information in one matrix and data from 111 female offspring of the Michigan fish-eater cohort are available (Table 1). Of the first sample, 35 women had serum samples analyzed for HOC, 35 have HOC data on placental samples, and 25 have HOC information on breast milk samples. Of the pregnant women 47.7% had eaten sport-caught fish for more than 10 years. In female offspring of fish-eaters this proportion was higher (81.1%).

Since serum levels are available in pregnant women and adult female offspring of the Michigan fish-eater, a comparison of the HOC burden cohort was feasible. Figure 1 shows that the concentration of sum of PCBs in pregnant women is negligible and does not increase with age; in 11 of 35 participants, PCB was not detected. However, the concentration in offspring of Michigan fish-eaters increases with age. p,p'-DDE slightly increases with age in pregnant women (Figure 1, note the scale is twice the scale of Figure 1). It was not detected in 8 of 35 samples and its median value was 96.9 ng/fat, higher than that of the sum of PCBs (17.4 ng/g fat). In offspring of Michigan fish-eaters p,p'-DDE increases with age. In women 50 years and older, the median level is 1357.8 ng/g fat compared to 297.5 ng/g fat for the sum of PCBs.

The median PBDEs concentration in pregnant women was 107.8 ng/g fat, higher than that of p,p'-DDE. Interestingly, the PBDE concentration did not increase with age in female offspring of Michigan fish eaters (Figure 3), indicating that the new introduction of these substances in the food chain occurred recently and did not yet lead to bioaccumulation in humans. The PBB concentration in pregnant women from Michigan is higher than the concentration of PCB (87 compared to 17.4 ng/g fat). Surprisingly, the median PBB concentration in pregnant women was higher than the PBB concentration in female offspring of Michigan fish-eaters. This is indicative that PBB is available in the food chain of these younger women more than in the food chain of the fish-eaters' offspring.

In breast 25 milk samples, p,p'-DDE was not detected in 3 samples (12%), total PCB not in 9 samples (36%), PBB not in 4 samples (16%), and PBDE not in 14 samples (56%). Concentrations of HOCs in serum, placenta, and breast milk are higher in women who ever consumed sport caught fish, significantly only for sum of PBDE in placental tissues and for PBB in breast milk (Table 2).

In serum, p,p'-DDE is correlated with PCB, PBB, and PBDE (Table 3). In the placenta, PBB and the sum of PCBs are highly correlated. In breast milk most of the HOCs are not correlated, with the exception of PBB and PBDEs. The various HOCs are only weakly to moderately correlated across the different matrices (data not shown). Only p,p'-DDE levels in placental tissue can predict p,p'-DDE concentrations in breast milk.

Discussion

The study indicates that given the low concentrations in human samples of pregnant women, PCBs are no longer major exposure. However, DDE poses a major concern. Surprisingly, PBDEs concentrations are lower in primiparous pregnant women than in offspring of Michigan fish eaters, which may indicate that fish consumption in Michigan is a major source of PBDE. In agreement with hypothesis, PBDE concentrations in the placenta and in breast milk were found to be 3-4 times higher in pregnant women who consumed sport-caught fish compared to those who did not (Table 2). PBDE as a new emerging substance did not show an increase with age, indicating a lack of bioaccumulation. It is also surprising that PBB153 concentrations were found to be higher in pregnant women than in female offspring of Michigan fish-eaters. It is possible that PBB, which entered the food chain by accident, predominantly in Western Michigan, still contributes to local food sources.

The lack of correlation between concentrations of HOC in maternal serum, placental tissue, and breast milk sample indicates that information gathered from different matrices cannot substitute one another. However, a limitation is that maternal serum was collected in the first half

of the pregnancy, and placental tissue and breast milk four to five months later. It cannot be excluded, that the maternal metabolism during pregnancy changed the HOC distribution. However, Jaraczewska *et al.* also found only moderate rank correlations between maternal serum collected at the time of birth and breast milk.³⁰

The last study that compared HOC in maternal and cord serum and breast milk in Michigan samples was published in 1983.⁶ This is the first study since more than 20 years that compares HOC levels in a Michigan population using various samples. In our sample of pregnant women, we found median p,p'-DDE levels of 82.5 ng/g fat. These are lower than levels reported for Canada in 1996 (336 ng/g fat),⁵⁶ Poland in 2006 (634 ng/g) and for Australia in 2007 (217-378 ng/g),^{30,57} but comparable to recent findings in Finish and Danish women (77 and 137 ng/g lipid, respectively).⁵⁸

The median level of p,p'-DDE found in placentas was 56.9 ng/g lipid. This level is comparable to concentrations reported for Spanish women in 2007 (76.6 ng/g lipid),⁴⁰ and for Finish and Danish women in 2007 (21 and 47 ng/g lipid, respectively).⁵⁸ No comparable information can be found for PBB. The median level for the sum of PBDE in breast milk samples was 2.3 ng/g fat and is comparable with findings in Poland (2.0 and 2.5 ng/g fat).³⁰ Other mean levels were 2.1 and 4.0 ng/g fat in Sweden^{59,60} and 6.6 ng/fat in England.⁶¹ We were astonished that PBDE was detected in a cow milk sample that we included as control, since no other HOC exceeded the detection limit.

It is surprising that DDE, PBB, and PBDE rank first in concentrations in maternal serum, placental, and breast milk samples in women residing close to the shore of Lake Michigan and Lake Huron, since PCB is still seen as the major pollutant in fish.

Table 1 Characteristics of the participating women

		Pregnant women (n=45) %	Female offspring of the Michigan fish- eater cohort (n=111) %
Age:	<20 years	25.0	1.8
	≥20 - <30 years	56.8	24.3
	≥30 - <40 years	18.2	26.1
	≥40 - <50 years	-	35.1
	≥50 years	-	12.6
Ever eaten sport-caught fish		71.1	93.7
Years eating sport-caught fish	none	37.8	6.3
	1-10 years	15.6	12.6
	> 10 years	47.7	81.1

Table 2: Concentrations of p,p'-DDE, PCB-total, sum of PBDE, and PBB153 in breast milk samples

in ng/g lipid	Never eaten sport caught fish					Ever eaten sport caught fish					Kruskal-Wallis test p-value
	n	Mean	Median	5%-	95%-value	n	Mean	Median	5%-	95%-value	
Serum p,p'-DDE	10	90.4	85.1	46.3	128.6	24	155.9	101.6	40.1	445.8	0.25
Serum PCB-total	10	18.1	17.0	9.3	25.7	24	17.9	19.0	7.7	27.3	0.95
Serum PBB153	10	90.4	85.1	46.3	128.6	24	89.3	95.2	38.6	136.7	0.95
Serum sum of PBDE [∇]	2	128.0	128.0	96.3	159.7	9	162.0	109.2	83.4	491.9	1.00
Placenta p,p'-DDE	9	54.5	55.7	24.7	119.9	27	92.6	57.6	40.8	247.2	0.11
Placenta PCB-total	8	9.8	9.9	5.8	13.2	24	20.3	11.1	8.2	31.3	0.15
Placenta PBB153	9	38.0	43.7	5.5	65.8	27	59.5	54.1	11.1	131.2	0.18
Placenta sum of PBDE	9	30.2	15.0	11.1	98.7	27	45.9	34.1	12.9	158.2	0.047
Milk p,p'-DDE	5	63.5	74.8	18.5	114.2	19	150.7	95.8	7.9	853.5	0.24
Milk PCB-total	5	20.2	18.5	0.0	55.1	19	26.4	25.0	0.0	112.5	0.94
Milk PBB153	5	3.9	5.2	1.0	6.7	19	7.6	7.5	0.7	13.9	0.04
Milk sum of PBDE	5	5.3	1.9	1.4	19.5	19	22.8	3.0	0.8	154.0	0.17

∇ Sum of PBDE include the congeners 28, 47, 77, 85, 99, 100, 153, 154, 183

Table 3: Rank correlations (Spearman) of halogenated organic compounds in breast milk samples (n=25)

in ng/g lipid	serum PCB-total	serum PBB153	Serum sum of PBDE
Serum p,p'-DDE	0.734	0.734	0.657
	<0.001	<0.001	0.020
Serum PCB-total			0.406
			0.191
Serum PBB153			

in ng/g lipid	Placenta PCB-total	Placenta PBB153	Placenta sum of PBDE
Placenta p,p'-DDE	0.584	0.605	0.314
	<0.001	<0.001	0.062
Placenta PCB-total		0.839	0.520
		<0.001	0.002
Placenta PBB153			0.575

in ng/g lipid	Milk PCB-total	Milk PBB153	Milk sum of PBDE
Milk p,p'-DDE	0.268	0.153	-0.191
	p=20	p=0.47	p=0.36
Milk PCB-total		-0.104	0.179
		p=0.62	p=0.39
Milk PBB153			0.501
			p=0.01

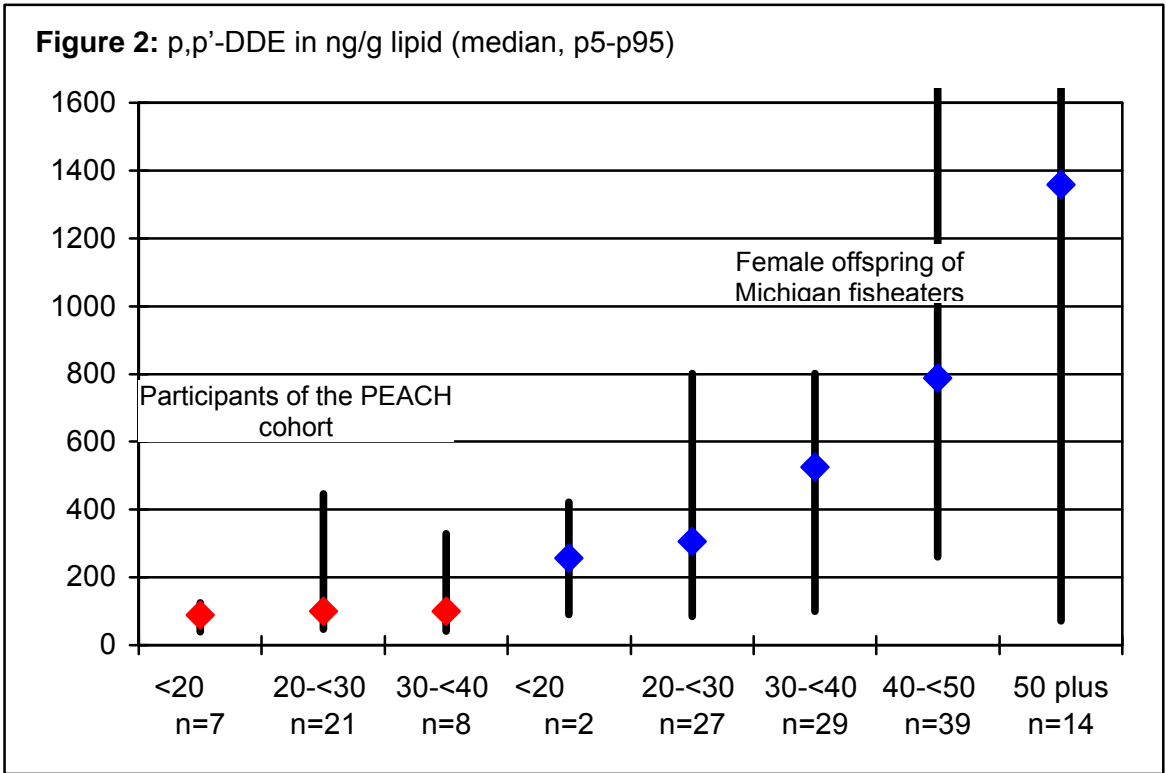
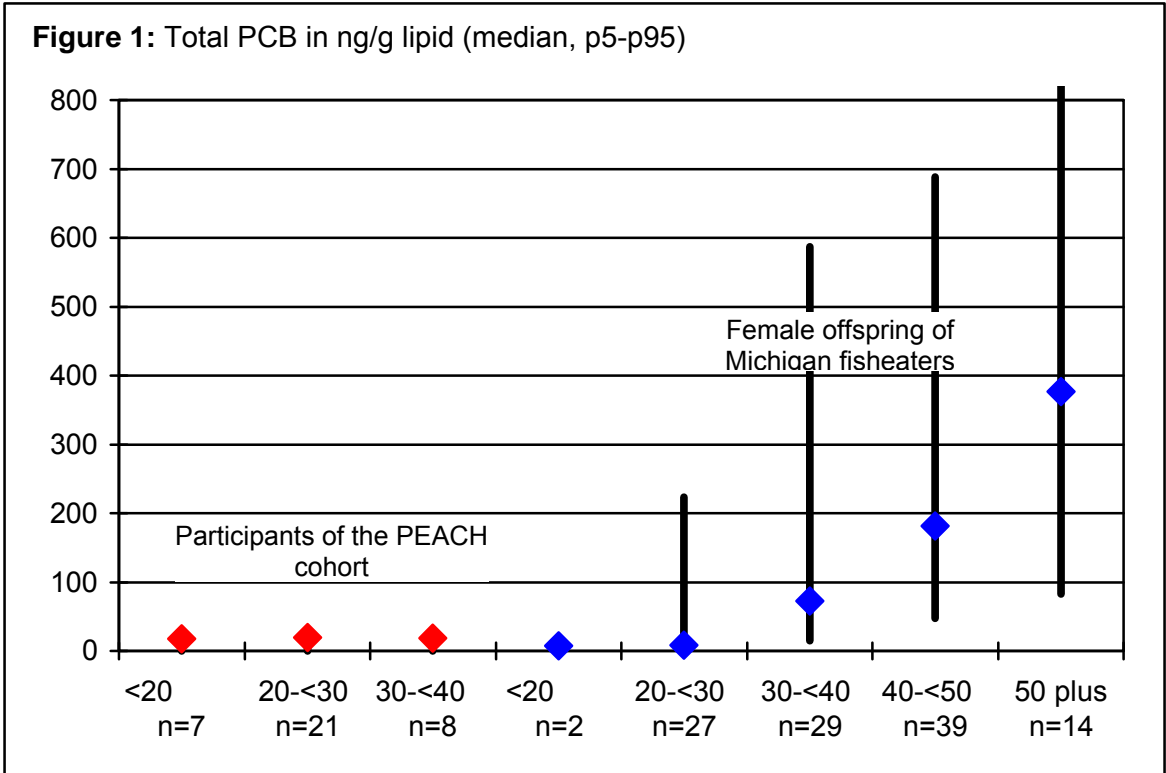


Figure 3: Sum of PBDE in ng/g lipid (median, p5-p95; congeners 28, 47, 77, 85, 99, 100, 153, 154, 183)

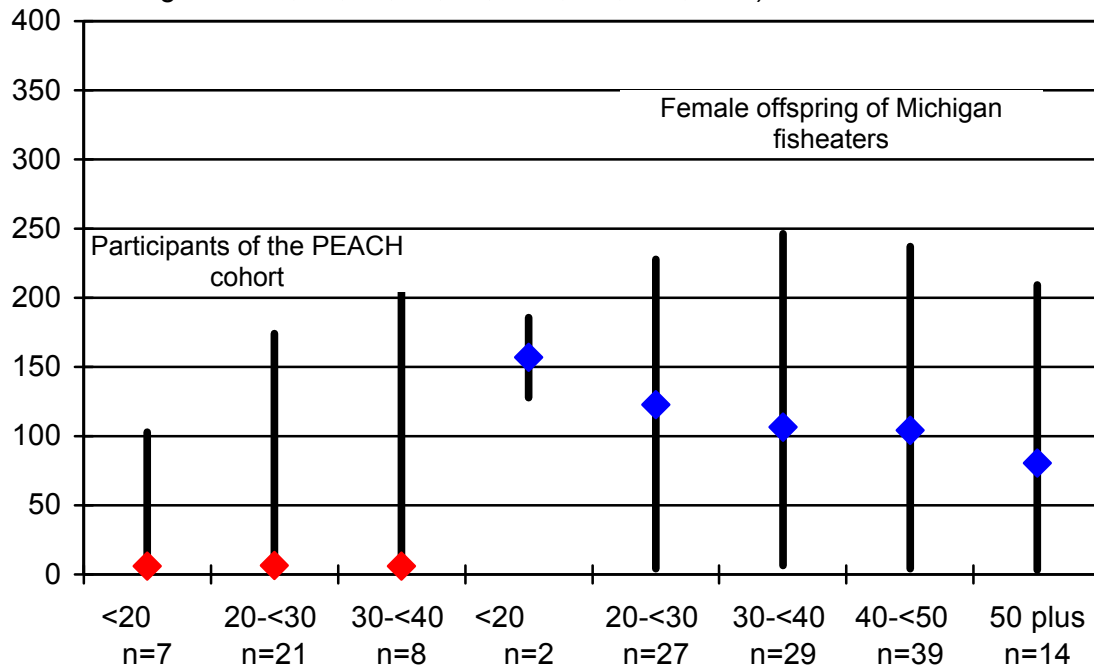


Figure 4: PBB153 in ng/g lipid (median, p5-p95)

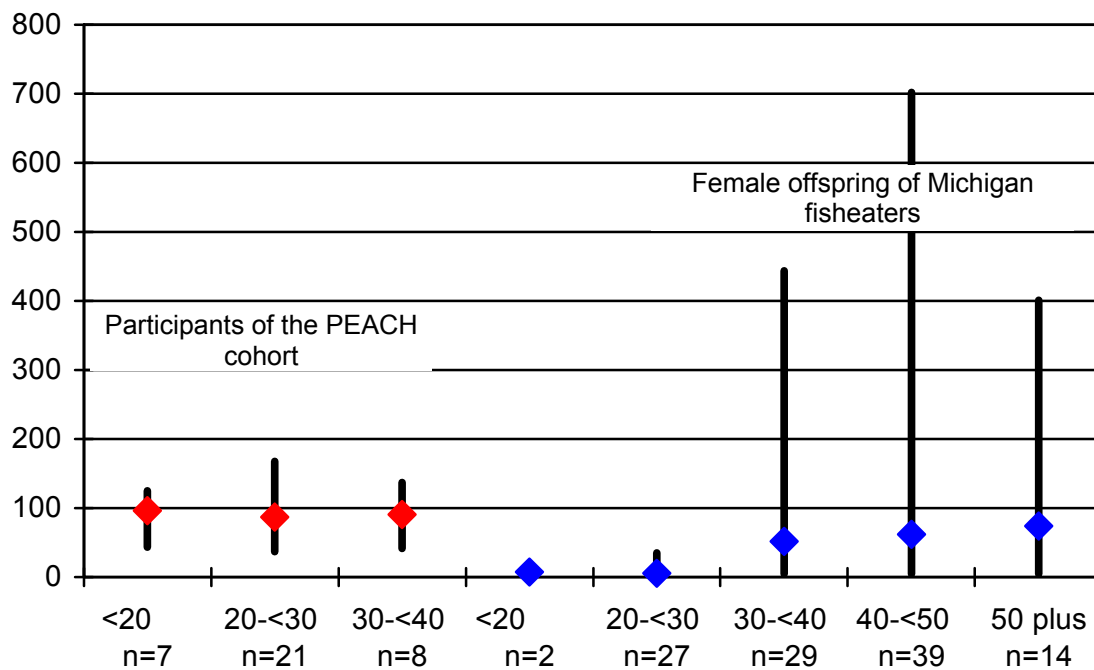
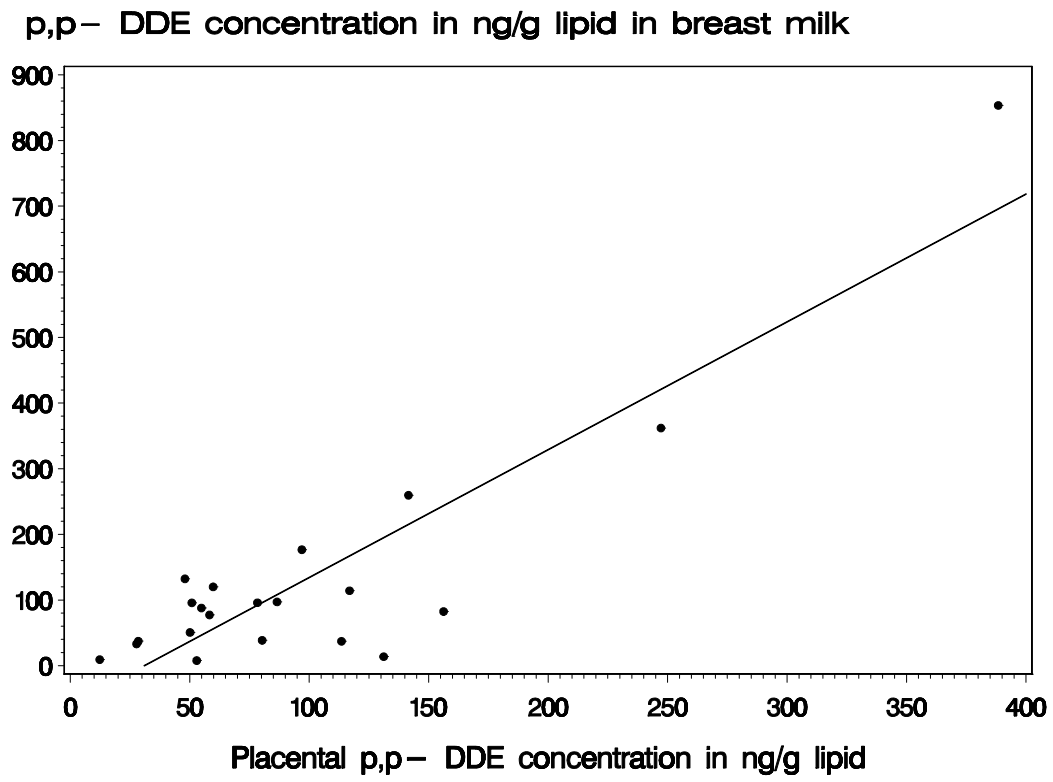


Figure 5: p,p'-DDE in breast milk and in placental samples



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