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RESEARCH ARTICLE

Anthropometric, socioeconomic, and maternal health determinants of placental transfer of organochlorine compounds

Henrieta Patayová · Soňa Wimmerová · Kinga Lancz · Ľubica Palkovičová · Beata Drobná · Anna Fabišiková · Ján Kováč · Irva Hertz-Picciotto · Todd A. Jusko · Tomáš Trnovec

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Abstract The aim of this study was to relate placental transfer, quantified by the cord to maternal serum concentration ratio (C/M), of five organochlorine pesticides (OCP) hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH), γ-hexachlorocyclohexane (γ-HCH) , *p*,*p*'-DDT, *p*,*p*'-DDE and 15 polychlorinated biphenyl (PCB) congeners (28, 52, 101, 105, 114, 118, 123^{+149}, 138^{+163}, 153, 156^{+171}, 157, 167, 170, 180, and 189) to anthropometric, socioeconomic, and maternal health characteristics. We included into the study 1,134 births during the period 2002–2004 from two districts in eastern Slovakia with high organochlorine concentrations relative to other areas of the world. Only concentrations >LOD were taken into account. Variables as age, weight and height of mothers, parity, ethnicity, alcohol consumption, illness during pregnancy, smoking during pregnancy, hypertension, respiratory diseases, rheumatoid arthritis and diabetes mellitus, and birth weight were related to C/M. Results of regression analyses showed that C/M was predicted by several factors studied. Positive associations were observed for gestational alcohol consumption, fewer illnesses during pregnancy, maternal age, and maternal weight. Caucasians had a greater C/M compared to Romani for wet weight data of congeners 170 and 180 and in contrast C/M for HCB was greater in Romani. Our results show that drinking mothers compared to abstaining expose their fetuses not only to alcohol but to an increased level of several PCB congeners. A straightforward explanation of associations between C/M shifts and factors studied is very difficult, however, with regard to the high lipophilicity of OCPs and PCBs, changes in their kinetics probably reflect lipid kinetics.

Keywords Placental transfer · Alcohol · PCB · Organochlorine pesticides

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H. Patayová · K. Lancz · Ľ. Palkovičová · T. Trnovec (✉)
Department of Environmental Medicine,
Slovak Medical University, Limbová 12,
83303 Bratislava, Slovakia
e-mail: tomas.trnovec@szu.sk

B. Drobná · A. Fabišiková
Department of Toxic Organic Pollutants,
Slovak Medical University, Limbová 12,
83303 Bratislava, Slovakia

S. Wimmerová
Institute of Biophysics, Informatics and Biostatistics,
Slovak Medical University, Limbová 12,
83303 Bratislava, Slovakia

J. Kováč
Department of Stomatology and Maxillofacial Surgery,
Comenius University, Faculty of Medicine in Bratislava, Špitálska 24,
81372 Bratislava, Slovakia

I. Hertz-Picciotto
Division of Epidemiology, Department of Public Health Sciences,
School of Medicine, University of California, Davis, CA, USA

T. A. Jusko
Epidemiology Branch, Department of Health and Human Services,
National Institute of Environmental Health Sciences, National
Institutes of Health, 111 T. W. Alexander Drive,
Research Triangle Park, NC 27709, USA

Introduction

Numerous studies show that exposure to environmental contaminants during fetal period or early childhood may cause long-term health effects such as increased susceptibility to cancer, damage to the immune and reproductive systems, and common chronic diseases in adult age. Low-level

exposures before or shortly after birth often produce more damaging and longer-lasting harm than exposures at higher levels in later childhood or adult life (Shonkoff and Garner 2012; Brent 2004; Shonkoff et al. 2009; Guyer et al. 2009; Hertz-Picciotto et al. 2008; Grandjean et al. 2008). Persistent Organic Pollutants (POPs) are ubiquitous chemicals found in many components of the environment. POPs include organochlorine pesticides (OCPs) and polychlorinated biphenyls (PCBs) which easily cross the placenta barrier, exposing humans during their early developmental stages. Assessment of prenatal exposure is very important in this connection and is mostly made indirectly by determining POP levels in umbilical cord blood (C). Information on placental transfer of POPs is obtained when C is related to concentration in maternal blood (M) at the time of delivery. Data on concentration of OCPs and PCBs and some of its metabolites in cord and maternal blood can be found in literature (Adetona et al. 2013; Porpora et al. 2013; Butler Walker et al. 2003; Bergonzi et al. 2011; 2009; Covaci et al. 2002; Tatsuta et al. 2012; Tsukimori et al. 2013a; 2013b; Nakano et al. 2005; Suzuki et al. 2005; Jacobson et al. 1984; Sala et al. 2001; Abballe et al. 2008). In spite of this wealth of information, the knowledge on maternal anthropometric, socioeconomic, and health factors which influence the transfer of POPs through human placenta is limited. The aim of this work was to study the association between placental transfer of several OCPs and PCB congeners and these factors. As a marker of placental transfer was used the cord/maternal serum concentration ratio (C/M) of the respective chemical.

Materials and methods

Between 2002–2004, 1,134 mothers were enrolled in a birth cohort study in eastern Slovakia (Hertz-Picciotto et al. 2003; Park et al. 2007). We collected blood samples from mothers delivering in the Michalovce and Svidnik district hospitals, eastern Slovakia. Michalovce district is home to a chemical manufacturing facility (Chemko, Strážske) that produced PCBs from 1959 to 1984. Of the 1,134 women enrolled in the study, maternal serum was available for organochlorine analysis on 1,103. All women provided written informed consent, and the study protocol was approved by institutional review boards at the University of California, Davis and the Slovak Medical University, Bratislava.

Whole maternal blood (20 ml) was collected from subjects just before delivery, allowed to clot, and centrifuged. Isolated serum was stored frozen at −18 °C until analysis. To collect cord blood, the infant was held at the level of the introitus on the mother's abdomen to prevent a significant shift of the infant's blood volume. As soon as possible after suctioning, the cord was clamped and cut 4–5 cm from the infant's abdomen. After the infant was dried and stabilized and the umbilical base appeared normal, an umbilical clamp was secured to the cord 1–2 cm distal to the abdominal wall, and any excess length was cut. Cord blood collection (30–35 ml) was done by the obstetrician or assisting nurse. All tubes of maternal and cord blood specimens were refrigerated at 5–10 °C immediately after collection. Samples were transported to the biochemistry department of each local hospital within 2 h for the next procedure. Serum was isolated by centrifugation and stored frozen at –18 °C till the analysis. During the mother's stay at the hospital, she was interviewed and asked to take a short IQ-like test (Raven's Progressive Matrices) (Raven and Raven 2002). Prior to discharge from the hospital, the mother was administered a questionnaire by a trained nurse and study coordinator. The maternal questionnaire collected information on the mothers' pregnancy, any complications, medications taken during pregnancy, previous pregnancy history, family medical history, lifestyle factors such as smoking and alcohol consumption, and sociodemographic, residential, household (number of rooms and number of people living there), gardening, environmental exposure, and employment and occupational information. Further questions addressed their diet, including nutritional variety and adequacy of micronutrient intake, consumption of locally or home-produced animal products, or locally caught fish. Data to be abstracted from medical charts included: month prenatal care began, gestational diabetes, complications during pregnancy, medications given during pregnancy or during labor and delivery, and anesthesia during labor and delivery.

Solid-phase extraction followed by clean-up procedure and high-resolution gas chromatography with micro-electron capture detection was used for analyses of OCPs and PCBs in human serum samples (Conka et al. 2005; Kocan et al. 1994). Serum mixed with an equivalent amount of water: 1-propanol (85:15, v/v) mixture was applied on a conditioned SPE column (2-g C18, endcapped, Alltech, Deerfield, Illinois, USA). The analytes were eluted with an n-hexane/dichloromethane (1:1, v/v) mixture, and the eluate was concentrated. The extract was cleaned up on a multilayer florisil–silica/H_2SO_4 column and eluted with hexane/dichloromethane (9:1, v/v). Isooctane was added as a keeper to the extract prior to concentration. Selected OCPs (hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH), γ-hexachlorocyclohexane (γ-HCH), *p*,*p*'-DDT, *p*,*p*'-DDE) and 15 PCB congeners (PCB-28, 52, 101, 105, 114, 118, 123^{+149}, 138^{+163}, $153{,}156^{+171}$, 157, 167, 170, 180, 189, IUPAC nos.) were analyzed using a Gas Chromatograph 6890N (Agilent Technologies, USA) equipped with a micro-electron capture detector, and an Agilent ChemStation software, splitless mode, injection volume 2 μl, a 60 m×0.25 mm ID×0.25 μm FT DB-5 (J&W Scientific, USA) capillary column. The following

temperature program was used: from initial temperature 110 °C (1.5 min) to 200 °C (0.2 min) at a rate of 30 and then 2.5°Cmin^{-1} to final temperature 305 °C (5 min). Five standard congener mixtures for 15 PCB congeners and 5 organochlorine pesticides established multilevel calibration curves. The method recovery was checked using PCB-174 as an internal standard. Only values ≥ limit of detection (LOD) were taken into account. Total serum lipids were estimated using enzymatic summation method (Akins et al. 1989). We report our results both on a lipid and non-lipid basis. C/M ratios were calculated for pairs in which data on concentration was available for both mother and her child.

Linear regression was used to determine the association between C/M and meaningful categorical or continuous predictors (parity, birth weight of the infant, mother age, height, weight, ethnicity, smoking and alcohol consumption during pregnancy, illnesses during pregnancy as diabetes mellitus, hypertension, arthritis, respiratory diseases). We considered the predictor as significant when p value was ≤0.05. Calculations were carried out with statistics program SPSS 16, Softonic International S.L.

Results

The overall cohort of newborn babies is described in Table 1. Those of Romani ethnicity represented 20.3 % of the study population. Thirty-five percent of the women in the study smoked prior to this pregnancy, 41 % were primipara, their mean gestational age was 39.6 weeks, and the mean birth

Table 1 Characteristics of the study groups in the cohort from two districts of eastern Slovakia, 2002–2004

	Category	Number (n)	Percent (%)
Maternal age	18–<20	95	8.2
	20–30	850	73.1
	>30	189	16.3
	Missing	28	2.4
Maternal weight (kg)	38–50	205	17.6
	51–68	590	50.8
	≥69	189	16.3
	Missing	178	15.3
Maternal height (cm)	133–159	207	17.8
	160–169	587	50.5
	≥170	241	20.7
	Missing	127	10.9
Gestation length (weeks)	<37	30	2.3
	37–<42	1,036	89.2
	≥42	32	2.8
	Missing	64	5.5
Birth weight (g)	<2,500	49	4.2
	2,500–<3,500	630	54.2
	≥3,500	427	36.7
	Missing	56	4.8
District	Michalovce	811	69.8
	Svidník	323	27.8
	Missing	28	2.4
	Total	1,162	100
Ethnicity	Slovakian	869	74.8
	Romani	326	20.3
	Missing	57	4.9
Maternal education M	Basic schooling	237	20.4
	High school without graduation	290	24.9
	High school with graduation	512	44.1
	More than College/ University	89	7.7
	Missing	34	2.9
Maternal smoking	No	726	62.5
	Yes	408	35.1
	Missing	28	2.4
Maternal alcohol consumption	No	936	80.6
	Yes	198	17
	Missing	28	2.4
Maternal diabetes history	No	1,121	96.5
	Yes	13	1.1
	Missing	28	2.4
Maternal respiratory history	No	917	78.9
	Yes	217	18.7
	Missing	28	2.4
Parity	0	471	40.5
	1	371	31.9
	2	196	16.9
	3	91	7.8
	4	2	0.2
	Missing	31	2.7
Sex of child	Male	573	49.3
	Female	534	46
	Missing	55	4.7
Exclusive breastfeeding duration (months)	0	44	3.8
	1–<6	868	74.7
	≥6	94	8.1
	Missing	156	13.4
Breastfeeding duration (months)	0	2	0.2
	1–6	640	55.1
	7–12	145	12.5
	>12	185	15.9
	Missing	190	16.4

weight was 3,327.9±499.1 g. The mean maternal age, weight, and height was 28.53±4.86 years, 60.05± 11.68 kg, and 164.53±6.25 cm, respectively.

The percentage of detection of OCPs and PCB congeners in maternal and cord blood serum samples is shown in Table 2. The concentration of OCPs was higher than the detection limit for most of samples except γ-HCH. From PCB congeners, only CB 118, 138^{+163}, 153, 156^{+171}, 170, and 180 could be detected in ≥60 % of samples. The wet weight or lipid adjusted concentration of the 5 pesticides and 15 PCB congeners investigated are shown in Table 3. The concentrations may be higher than in reality as means and medians were calculated from samples ≥ LOD. However, the focus of this study is on ratios C/M which were not biased by such proceeding. It can be seen that with lipid adjusted data most C/M values oscillate around 1, while with wet weight data, the values of C/M ratios were much smaller. This difference is due to high lipid solubility of this group of organochlorines and the much lower lipid concentration in fetal compared to maternal blood.

Table 4 summarizes results of multiple linear regression analysis which was used for identification of factors associated with C/M ratio. B is regression coefficient and the negative sign of regression coefficient means that the variables are negatively associated. We present only regression results in which $p \leq 0.05$. Unexpectedly, the strongest predictor of C/M was alcohol intake during pregnancy. Alcohol consumption explained a C/M increase for six PCB congeners, all with high percentage of detection, when data were expressed as wet weight and for two congeners when data were lipid adjusted. Thus, mothers not consuming alcohol during pregnancy had lower C/M values compared to mothers consuming alcohol, except PCB 189 with which the effect was opposite, however, on margin of significance. For pesticides alcohol was a predictor of increasing C/M value only with γ-HCH derived from wet weight data. The effect of smoking was observed with HCB. Smoking also predicted a decrease of lipid adjusted C/M for γ-HCH. Disease during pregnancy explained decreased C/M ratio for wet weight β-HCH and PCB 156^{+171}. C/M for PCB 157, a congener with high detection percentage after both modes of expression, was greater in primiparas when compared to secundiparas and multiparas. On the contrary, for lipid adjusted β-HCH and γ-HCH, multiparity predicted higher levels compared to secundi and primiparity. Being a Romani means a lower C/M for PCB 170 and PCB 180 with wet weight data. On the other hand, Romani ethnicity does not protect before HCB. Birth weight predicted a decreased C/M for 138^{+163}, 170, 180, 189 and DDE. Mother weight and age were slight predictors of C/M. Mother weight predicted an increased C/M ratio for PCB 189 and age for congeners PCB 105 and PCB 170, however, of these congeners, only PCB 170 has a high percentage of detection. Total lipids significantly predicted a decreased C/M for PCB congeners 118, 138^{+163}, 156^{+171}, 170, 180, and 189, all with high percentage of detection except PCB 189.

Discussion

Placental transfer of many environmentally and pharmacologically important compounds has been studied in vivo, by ex vivo human placental perfusion and more recently by quantitative structure–activity relationship methodology taking into account the molecular, physicochemical, and structural properties (Giaginis et al. 2011; Correia Carreira et al. 2011; Vähäkangas and Myllynen 2009; Giaginis et al. 2009; Myllynen et al. 2005; Myren et al. 2007). With regard to high lipid solubility, neutral character, limited protein binding, and rather small molecular size, the OCPs and PCBs pass the placenta barrier easily by means of passive diffusion.

The knowledge on anthropometric, maternal health or socioeconomic factors predicting toxicokinetics of OCPs and PCBs is abundant. The most important descriptors of behavior of these compounds in the body which have been studied are maternal age, education status, body height, prepregnancy weight, weight gain and BMI, gestational length, parity, diseases as diabetes, hypertension and preeclampsia, alcohol and smoking habits during pregnancy, maternal

Table 2 Percentage of samples with concentration of OCPs and PCB congeners≥LOD

	Mother	Cord	Mother	Cord	Mother	Cord	Mother	Cord	Mother	Cord
Pesticide	β-HCH		γ-HCH		HCB		p,p′-DDE		p,p′-DDT	
% of detection	85.9	82.9	27	24	96.3	96.3	99.7	99.3	96.3	97.7
PCB congener	28		52		101		105		114	
% of detection	38.8	12.8	14.5	12.5	19.3	19.7	18.8	7.2	13.3	4.4
PCB congener	118		123^{+149}		138^{+163}		153		156^{+171}	
% of detection	83.6	69.4	14	12.3	100	99.4	100	99.8	95.5	67.5
PCB congener	157		167		170		180		189	
% of detection	18.9	7	51.9	18	99.8	98.7	100	99.9	30.8	12.3

Table 3 Concentration of organochlorine pesticides and PCB congeners studied in serum samples from umbilical cord blood and maternal blood

Concentration		Cord	Mother	Cord	Mother	Cord	Mother	Cord	Mother	Cord	Mother
Pesticide		β-HCH		γ-HCH		HCB		p,p′-DDE		p,p′-DDT	
Wet weight ng/ml serum	*n*	882	926	256	281	1,027	1,038	1,069	1,085	1,052	1,031
	Mean±SD	0.029±0.026	0.116±0.113	0.011±0.008	0.02±0.02	0.291±0.467	1.139±1.96	1.306±1.183	5.53±4.825	0.063±0.083	0.315±0.315
	n ratio	755		50		931		1,011		952	
	Mean ratio±SD	0.286±0.294		0.727±0.938		0.342±0.645		0.255±0.198		0.242±0.829	
	Median ratio	0.242		0.47		0.265		0.227		0.191	
Lipid adjusted ng/g lipid	*n*	882	926	256	281	1,027	1,038	1,069	1,085	1,052	1,031
	Mean±SD	11.3±10.4	11.3±10.5	4.45±4.67	2.03±1.87	117.3±183.7	108.7±163.8	521.1±448.3	533.3±426.9	24.6±25.4	30.6±29.3
	Median	8.61	9.193	3.307	1.431	73.989	68.097	393.348	426.769	17.427	21.41
	n ratio	755		50		931		1011		952	
	Mean ratio±SD	1.189±1.903		0.578±0.749		1.373±2.408		1.021±1.021		0.898±1.205	
	Median ratio	0.993		0.292		1.097		0.938		0.798	
PCB congener		28		52		101		105		114	
Wet weight ng/ml serum	*n*	136	409	133	161	212	213	78	219	47	146
	Mean±SD	0.033±0.038	0.087±0.154	0.022±0.025	0.075±0.234	0.110±1.155	0.068±0.108	0.018±0.023	0.056±0.114	0.014±0.011	0.030±0.065
	n ratio	88		20		59		54		16	
	Mean ratio±SD	0.384±0.558		0.503±0.675		0.585±0.769		0.381±0.627		0.601±0.686	
	Median ratio	0.228		0.269		0.37		0.187		0.289	
Lipid adjusted ng/g lipid W	*n*	134	404	130	157	211	210	75	216	47	144
	Mean±SD	12.59±10.72	7.96±10.50	7.78±5.21	5.35±4.68	12.73±15.91	6.13±6.63	5.98±4.36	4.49±5.45	5.89±5.44	2.36±3.49
	Median	9.001	4.588	6.451	3.964	8.601	4.244	4.56	3.051	3.608	1.487
	n ratio	88		20		59		24		16	
	Mean ratio±SD	1.439±1.654		2.598±4.023		2.332±2.695		1.531±2.497		2.806±3.235	
	Median ratio	1.062		1.215		1.315		0.674		1.157	
PCB congener		118		123^{149}		138^{+163}		153		156^{+171}	
Wet weight ng/ml serum	*n*	749	920	133	154	1,074	1,099	1,078	1,099	729	1,051
	Mean±SD	0.037±0.066	0.167±0.301	0.021±0.058	0.036±0.043	0.284±0.364	1.237±1.218	0.389±0.454	1.881±1.703	0.025±0.034	0.179±0.292
	Median	0.018	0.101	0.011	0.02	0.187	0.877	0.269	1.378	0.015	0.113
	n ratio	639		57		1,016		1,020		662	
	Mean ratio±SD	0.195±0.201		0.511±0.560		0.224±0.171		0.200±0.097		0.150±0.155	
	Median ratio	0.163		0.336		0.2		0.185		0.118	
Lipid adjusted ng/g lipid	*n*	747	909	132	154	1,072	1,089	1,076	1,091	726	1,037
	Mean±SD	13.68±18.67	15.60±18.53	6.63±8.67	3.38±3.77	110.5±120.6	124.6±155.6	152.1±151.4	191.8±224.7	9.47±10.74	16.14±17.06
	Median	7.379	9.958	4.425	1.997	74.328	87.427	108.729	138.044	5.834	11.299

Table 3 (continued)

Concentration		Cord	Mother	Cord	Mother	Cord	Mother	Cord	Mother	Cord	Mother
	n ratio	639		57		1016		1021		662	
	Mean ratio±SD	0.768±0.733		2.273±2.862		0.894±0.716		0.808±0.568		0.577±0.510	
	Median ratio	0.681		1.398		0.828		0.755		0.485	
PCB congener		157		167		170		180		189	
Wet weight ng/ml serum	*n*	76	208	194	571	1,066	1,099	1,079	1,098	339	339
	Mean±SD	0.015±0.012	0.040±0.059	0.030±0.064	0.082±0.219	0.135±0.173	0.783±1.041	0.328±0.405	1.761±1.679	0.014±0.014	0.044±0.066
	Median	0.011	0.024	0.015	0.043	0.087	0.527	0.213	1.241	0.009	0.03
	n ratio	46		157		1,006		1,022		92	
	Mean ratio±SD	0.719±0.960		0.224±0.212		0.169±0.083		0.177±0.078		0.438±0.553	
	Median ratio	0.331		0.172		0.155		0.166		0.246	
Lipid adjusted ng/g lipid	*n*	75	203	193	565	1,062	1,085	1,075	1,091	131	330
	Mean±SD	5.81±4.54	3.47±3.79	10.78±16.15	7.04±11.06	51.40±53.37	72.63±68.17	125.9±127.4	180.4±207.8	5.132±4.115	3.777±3.628
	Median	4.005	2.442	6.144	4.12	35.446	52.192	86.19	124.11	3.604	2.679
	n ratio	46		157		1006		1023		92	
	Mean ratio±SD	3.093±3.938		0.920±0.842		0.666±0.257		0.716±0.420		1.797±2.326	
	Median ratio	1.218		0.744		0.654		0.68		0.99	

Means and medians were calculated for serum concentrations and for the cord to maternal serum concentrations ratios. Wet weight and lipid adjusted data are presented

Table 4 Results of the multiple linear regression analysis

		Wet weight			Lipid adjusted		
Parameter	Congener	B	Std. Error	Sig.	B	Std. Error	Sig
Alcohol consumption	γ-HCH	−1.117	0.508	0.035			
	PCB 118	−0.050	0.023	0.033			
	PCB 138^{+163}	−0.045	0.015	0.003			
	PCB 156^{+171}	−0.045	0.017	0.010	−0.142	0.058	0.016
	PCB 180	−0.016	0.006	0.009			
	PCB 170	−0.018	0.007	0.009	−0.055	0.023	0.017
	PCB 189	0.390	0.189	0.043			
	PCB 153	−0.023	0.008	0.004			
Smoking during pregnancy	γ-HCH				0.853	0.320	0.012
	HCB	0.106	0.053	0.044	0.626	0.285	0.028
	PCB 123^{+149}	−0.556	0.232	0.024	−2.798	1.261	0.035
Disease during pregnancy	β-HCH	0.054	0.027	0.044			
	PCB 123^{+149}	1.138	0.215	0.000	6.047	1.168	0.000
	PCB 156^{+171}				0.100	0.049	0.041
Diabetes	HCB	−0.625	0.128	0.000	−3.849	0.692	0.000
Primipara vs. multipara	β-HCH				−0.846	0.365	0.021
	γ-HCH				−1.954	0.707	0.009
	PCB 157	1.958	0.908	0.042	8.243	3.639	0.033
Primipara vs. secundipara	PCB 123^{+149}	−0.447	0.216	0.048			
	PCB 157	1.193	0.521	0.031	5.005	2.025	0.021
Secundipara vs. multipara	β-HCH				−0.852	0.351	0.015
	γ-HCH				−1.594	0.691	0.027
	PCB 123^{+149}	1.137	0.363	0.004	5.480	1.900	0.007
	PCB 114	−1.059	0.234	0.045			
Romani	HCB	−0.105	0.052	0.044	−0.861	0.280	0.002
	PCB 123^{+149}	0.517	0.249	0.047	3.099	1.313	0.025
	PCB 180	0.024	0.008	0.002			
	PCB 170	0.024	0.008	0.005			
Birth weight	DDE	−0.000032	0.000016	0.040			
	PCB 123^{+149}	0.00043	0.00019	0.034	0.002	0.001	0.032
	PCB 138^{163}	−0.00004	0.00001	0.002			
	PCB 180	−0.00003	0.00001	0.000			
	PCB 170	−0.00003	0.00001	0.000	0.000	0.000	0.001
	PCB 189	-0.00003	0.00001	0.000			
Mother weight	γ-HCH				−0.038	0.012	0.004
	PCB 189	0.014	0.006	0.036			
Mother age	PCB 105	0.040	0.013	0.005	0.190	0.056	0.002
	PCB 170				0.008	0.002	0.001
Total lipid content mg/mL	HCB	−0.036	0.008	0.000			
	DDE	−0.021	0.003	0.000			
	PCB 118	−0.014	0.004	0.003			
	PCB 138^{+163}	−0.018	0.003	0.000			
	PCB 156^{+171}	−0.014	0.003	0.000			
	PCB 180	−0.012	0.001	0.000			
	PCB 170	−0.012	0.001	0.000			
	PCB 189	−0.015	0.002	0.000			

The dependent variables were the umbilical cord to mother blood serum concentration ratio of 5 organochlorinated pesticides and 15 PCB congeners and the independent variables various anthropometric, socioeconomic, and health characteristics of mother (parity, mother age, height, weight, ethnicity, smoking during pregnancy, alcohol consumption during pregnancy, diabetes mellitus, hypertension, respiratory diseases, arthritis, illness during pregnancy, birth weight of the infant, total serum lipid concentration in maternal blood)

occupation, place of residence, fuel type used for cooking, and marital status. From newborn variables interactions with sex, weight, length, head circumference, and Apgar score were described (Glynn et al. 2007; Llop, et al. 2010; Hansen et al. 2010; Adetona et al. 2013; Bergonzi et al. 2009; 2011; Freire et al. 2011; Arrebola et al. 2010; 2012a; 2012b; 2012c). To our knowledge, however, none of these determinants has so far been related to placental transfer of OCPs or PCBs. Nevertheless, some of these aforementioned factors may be even indirectly related to the process of placental transfer of organochlorines.

In our analysis, we have observed different signs of regression coefficient B for some OCPs and PCB congeners showing which variables are positively or negatively associated. This diversity in behavior can be explained by structural differences within OCPs and PCBs and by different physicochemical properties which determine their behavior within biological systems. Of factors potentially influencing C/M, parity is worth mentioning. A negative relationship was found between levels of some PCB congeners in cord blood and parity (Llop, et al. 2010), however, in this study, the cord blood concentrations were not paired with maternal blood concentrations which is needed for estimation of C/M, a marker of placental transfer. Another factor deserving comment is placental uptake of organochlorines which could also be indirectly related to placental transfer. Thus dioxins, structurally related to OCPs and PCBs, have been shown to accumulate in the placenta (Suzuki et al. 2005), however, the transfer of these compounds from maternal to cord blood was independent of placental accumulation (Tsukimori et al. 2013b). From anthropometric measures, higher maternal body mass index was significantly associated with higher endosulfan, a member of OCPs, concentrations in placenta, and greater maternal weight gain was significantly associated with higher *p*,*p*'-DDE concentrations (Lopez-Espinosa et al. 2007). Unfortunately, information on the simultaneous cord blood concentration is not available.

To explain the association between lower C/M and observed lower birth weight is very difficult. However, with regard to the high lipophilicity of PCBs, changes in their kinetics usually reflect lipid kinetics. Lower birth weight mostly reflects reduced placenta transfer of nutrients, including lipids. Although ethanol abuse and smoking during pregnancy are in focus of interest due to reduced growth of human fetus and other detrimental effects, the information on their effect on passage of toxic chemicals across the placenta is rather small. Thus evaluated was their effect on transport of vitamins or nutrients necessary for growth of the fetus (Jauniaux et al. 2007; Haggarty et al. 2002; Schenker et al. 1989) or DNA oxidation products (Rossner et al. 2009). In view of this, the association between alcohol consumption and C/M for several PCB congeners may be of toxicological interest, as this is very probably the first finding of ethanol effect on enhanced placental transfer of toxicologically interesting substances. So far, it was reported that alcohol consumption does not have any effect on placental transfer of some indicator substances (Veid et al. 2011; Phillips 1981). Noticeably, for almost the same group of PCB congeners of which C/M is associated with drinking, there was a positive association between total concentration of serum lipids and C/M. In other words, an increase of total serum lipid level predicted a decrease of C/M for the same congeners as those associated with alcohol consumption. With regard to high lipophilicity of PCBs, the C/M shifts in association with alcohol may be secondary to the effect of alcohol on lipid metabolism. The effect of alcohol drinking on lipid metabolism is well known (Hata and Nakajima 2000; Hendriks et al. 1998; 2001; Brien et al. 2011). Nevertheless, disregarding the mode of action, the overall alcohol effect is important as the drinking compared to the abstaining mother exposes her fetus not only to alcohol but to an increased level of several PCB congeners.

The key finding of our study is that the anthropometric, socioeconomic, and maternal health factors are associated not only with functioning of main organs like intestines, liver, and kidneys, determining the kinetics of the OCPs and PCBs in the body, but also with functioning of a small but relatively extremely important part of the body system, the placenta. For most of the OCPs and PCB congeners placenta presents a very weak barrier as seen from the ratio of their maternal to cord blood serum concentration slightly over 1. Existence of factors worsening even that faint barrier function has been shown.

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References

Abballe A, Guarino M, Taggi F, Traina ME, Urbani E, Valentini S, De Felip E (2008) Maternal blood levels of persistent organic pollutants can be used to estimate in utero exposure. Ann Ist Super Sanita 44(3):281–291

Adetona O, Horton K, Sjodin A, Jones R, Hall DB, Aguillar-Villalobos M, Cassidy BE et al (2013) Concentrations of select persistent organic pollutants across pregnancy trimesters in maternal and in cord serum in Trujillo, Peru. Chemosphere 91(10):1426–1433. doi:10.1016/j.chemosphere.2013.01.043, Epub 2013 Feb 28

Akins JR, Waldrep K, Bernert JT Jr (1989) The estimation of total serum lipids by a completely enzymatic 'summation' method. Clin Chim Acta 184:219–226

Arrebola JP, Fernandez MF, Porta M, Rosell J, de la Ossa RM, Olea N, Martin-Olmedo P (2010) Multivariate models to predict human adipose tissue PCB concentrations in Southern Spain. Environ Int 36(7):705–713

Arrebola JP, Mutch E, Rivero M, Choque A, Silvestre S, Olea N, Ocaña-Riola R, Mercado LA (2012a) Contribution of sociodemographic characteristics, occupation, diet, and lifestyle to DDT and DDE concentrations in serum and adipose tissue from a Bolivian cohort. Environ Int 38(1):54–61

Arrebola JP, Cuellar M, Claure E, Quevedo M, Antelo SR, Mutch E, Ramirez E, Fernandez MF, Olea N, Mercado LA (2012b) Concentrations of organochlorine pesticides and polychlorinated biphenyls in human serum and adipose tissue from Bolivia. Environ Res 112:40–47

Arrebola JP, Mutch E, Cuellar M, Quevedo M, Claure E, Mejía LM, Fernández-Rodríguez M, Freire C, Olea N, Mercado LA (2012c) Factors influencing combined exposure to three indicator polychlorinated biphenyls in an adult cohort from Bolivia. Environ Res 116:17–25

Bergonzi R, Specchia C, Dinolfo M, Tomasi C, De Palma G, Frusca T, Apostoli P (2009) Distribution of persistent organochlorine pollutants in maternal and foetal tissues: data from an Italian polluted urban area. Chemosphere 76(6):747–754

Bergonzi R, De Palma G, Specchia C, Dinolfo M, Tomasi C, Frusca T, Apostoli P (2011) Persistent organochlorine compounds in fetal and maternal tissues: evaluation of their potential influence on several indicators of fetal growth and health. Sci Total Environ 409(15):2888–2893

Brent RL (2004) Environmental causes of human congenital malformations: the pediatrician's role in dealing with these complex clinical problems caused by a multiplicity of environmental and genetic factors. Pediatrics 113:957–968

Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA (2011) Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies. BMJ. doi:10.1136/bmj.d636

Butler Walker J, Seddon L, McMullen E, Houseman J, Tofflemire K, Corriveau A, Weber JP, Mills C, Smith S, Van Oostdam J (2003) Organochlorine levels in maternal and umbilical cord blood plasma in Arctic Canada. Sci Total Environ 1–3:27–52

Conka K, Drobna B, Kocan A, Petrik J (2005) Simple solid-phase extraction method for determination of polychlorinated biphenyls and selected organochlorine pesticides in human serum. J Chromatogr A 1084:33–38

Correia Carreira S, Cartwright L, Mathiesen L, Knudsen LE, Saunders M (2011) Studying placental transfer of highly purified non-dioxin-like PCBs in two models of the placental barrier. Placenta 32:283–291

Covaci A, Jorens P, Jacquemyn Y, Schepens P (2002) Distribution of PCBs and organochlorine pesticides in umbilical cord and maternal serum. Sci Total Environ 298(1–3):45–53

Freire C, Amaya E, Fernández MF, González-Galarzo MC, Ramos R, Molina-Molina JM, Arrebola JP, Olea N (2011) Relationship between occupational social class and exposure to organochlorine pesticides during pregnancy. Chemosphere 83(6):831–838

Giaginis C, Zira A, Theocharis S, Tsantili-Kakoulidou A (2009) Application of quantitative structure–activity relationships for modeling drug and chemical transport across the human placenta barrier: a multivariate data analysis approach. J Appl Toxicol 29:724–733

Giaginis C, Tsantili-Kakoulidou A, Theocharis S (2011) Assessing drug transport across the human placental barrier: from in vivo and in vitro measurements to the ex vivo perfusion method and in silico techniques. Curr Pharm Biotechnol 12:804–813

Glynn A, Aune M, Darnerud PO, Cnattingius S, Bjerselius R, Becker W, Lignell S (2007) Determinants of serum concentrations of organochlorine compounds in Swedish pregnant women: a cross-sectional study. Environ Health 6:2

Grandjean P, Bellinger D, Bergman A et al (2008) The Faroes statement: human health effects of developmental exposure to chemicals in our environment. Basic Chem Pharmacol Toxicol 102:73–75

Guyer B, Ma S, Grason H, Frick K, Perry D, Sharkey A, McIntosh J (2009) Early childhood health promotion and its life-course health consequences. Acad Pediatr 9:142–149

Haggarty P, Abramovich DR, Page K (2002) The effect of maternal smoking and ethanol on fatty acid transport by the human placenta. Br J Nutr 87(3):247–252

Hansen S, Nieboer E, Odland JŘ, Wilsgaard T, Veyhe AS, Sandanger TM (2010) Levels of organochlorines and lipids across pregnancy, delivery and postpartum periods in women from Northern Norway. J Environ Monitor 12(11):2128–2137

Hata Y, Nakajima K (2000) Life-style and serum lipids and lipoproteins. J Atheroscler Thromb 7:177–197

Hendriks HF, Veenstra J, van Tol A, Groener JE, Schaafsma G (1998) Moderate doses of alcoholic beverages with dinner and postprandial high density lipoprotein composition. Alcohol Alcohol 33:403–410

Hendriks HF, van Haaren MR, Leenen R, Schaafsma G (2001) Moderate alcohol consumption and postprandial plasma lipids in men with different risks for coronary heart disease. Alcohol Clin Exp Res 25:563–270

Hertz-Picciotto I, Trnovec T, Kocan A, Charles MJ, Ciznar P, Langer P, Sovcikova E, James R (2003) PCBs and early childhood development in Slovakia: study design and background. Fresen Environ Bull 12:208–214

Hertz-Picciotto I, Park HY, Dostal M, Kocan A, Trnovec T, Sram R (2008) Prenatal exposures to persistent and non-persistent organic compounds and effects on immune system development. Basic Clin Pharmacol Toxicol 102:146–154

Jacobson JL, Fein GG, Jacobson SW, Schwartz PM, Dowler JK (1984) The transfer of polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs) across the human placenta and into maternal milk. Am J Public Health 74:378–379

Jauniaux E, Johns J, Gulbis B, Spasic-Boskovic O, Burton GJ (2007) Transfer of folic acid inside the first-trimester gestational sac and the effect of maternal smoking. Am J Obstet Gynecol 197(1):58.e1–58.e6

Kocan A, Petrik J, Drobna B, Chovancova J (1994) Levels of PCBs and some organochlorine pesticides in the human population of selected areas of the Slovak Republic. Chemosphere 29:2315–2325

Llop S, Ballester F, Vizcaino E, Murcia M, Lopez-Espinosa MJ, Rebagliato M, Vioque J, Marco A, Grimalt JO (2010) Concentrations and determinants of organochlorine levels among pregnant women in eastern Spain. Sci Total Environ 408(23):5758–5767

Lopez-Espinosa MJ, Granada A, Carreno J, Salvatierra M, Olea-Serrano F, Olea N (2007) Organochlorine pesticides in placentas from southern Spain and some related factors. Placenta 28(7):631–638

Myllynen P, Pasanen M, Pelkonen O (2005) Human placenta: a human organ for developmental toxicology research and biomonitoring. Placenta 26:361–371

Myren M, Mose T, Mathiasen L, Knudsen L (2007) The human placenta—an alternative for studying foetal exposure. Toxicol 21:1332–1340

Nakano S, Noguchi T, Takekoshi H, Suzuki G, Nakano M (2005) Maternal-fetal distribution and transfer of dioxins in pregnant women in Japan, and attempts to reduce maternal transfer with Chlorella (*Chlorella pyrenoidosa*) supplements. Chemosphere 61(9):1244–1255

Park JS, Linderholm L, Charles MJ, Athanasiadou M, Petrik J, Kocan A, Drobna B, Trnovec T, Bergman A, Hertz-Picciotto I (2007) Polychlorinated biphenyls and their hydroxylated metabolites (OH-PCBS) in pregnant women from eastern Slovakia. Environ Health Perspect 115:20–27

Phillips SC (1981) Does ethanol damage the blood–brain barrier? J Neurol Sci 50:81–87

Porpora MG, Lucchini R, Abballe A, Ingelido AM, Valentini S, Fuggetta E, Cardi V, Ticino A, Marra V, Fulgenzi AR, Felip ED (2013) Placental transfer of persistent organic pollutants: a preliminary study on mother–newborn pairs. Int J Environ Res Public Health 10(2):699–711

Raven J, Raven JC (2002) Manual for Raven's Progressive Matrices and vocabulary scales. San Antonio, TX: Harcourt Assessment, update: Raven intelligence test for adults (uncolored progressive matrices), Publ. Psychodiagnostika, a.s. Bratislava, Catalog: 2000/2002 (in Slovak)

Rossner P Jr, Milcova A, Libalova H, Novakova Z, Topinka J, Balascak I, Sram RJ (2009) Biomarkers of exposure to tobacco smoke and environmental pollutants in mothers and their transplacental transfer to the foetus. Part II. Oxidative damage. Mutat Res 669(1–2):20–26

Sala M, Ribas-Fitó N, Cardo E, de Muga ME, Marco E, Mazón C, Verdú A, Grimalt JO, Sunyer J (2001) Levels of hexachlorobenzene and other organochlorine compounds in cord blood: exposure across placenta. Chemosphere 43(4–7):895–901

Schenker S, Johnson RF, Hays SE, Ganeshappa R, Henderson GI (1989) Effects of nicotine and nicotine/ethanol on human placental amino acids transfer. Alcohol 6(4):289–296

Shonkoff JP, Garner AS (2012) The lifelong effects of early childhood adversity and toxic stress. Pediatrics 129:e232–246

Shonkoff JP, Boyce WT, McEwen BS (2009) Neuroscience, molecular biology, and the childhood roots of health disparities: building a new framework for health promotion and disease prevention. JAMA 301:2252–2259

Suzuki G, Nakano M, Nakano S (2005) Distribution of PCDDs/PCDFs and co-PCBs in human maternal blood, cord blood, placenta, milk, and adipose tissue: dioxins showing high toxic equivalency factor accumulate in the placenta. Biosci Biotechnol Biochem 69(10):1836–1847

Tatsuta N, Nakai K, Murata K, Suzuki K, Iwai-Shimada M, Yaginuma-Sakurai K, Kurokawa N, Nakamura T, Hosokawa T, Satoh H (2012) Prenatal exposures to environmental chemicals and birth order as risk factors for child behavior problems. Environ Res 114:47–52

Tsukimori K, Uchi H, Tokunaga S, Yasukawa F, Chiba T, Kajiwara J, Hirata T, Furue M (2013a) Blood levels of PCDDs, PCDFs, and coplanar PCBs in Yusho mothers and their descendants: association with fetal Yusho disease. Chemosphere 90(5):1581–1588

Tsukimori K, Morokuma S, Hori T, Takahashi K, Hirata T, Otera Y, Fukushima K, Kawamoto T, Wake N (2013b) Characterization of placental transfer of polychlorinated dibenzo-p-dioxins, dibenzofurans, and polychlorinated biphenyls in normal pregnancy. J Obstet Gynaecol Res 39(1):83–90

Vähäkangas K, Myllynen P (2009) Drug transporters in the human blood-placental barrier. Br J Pharmacol 158:665–678

Veid J, Karttunen V, Myöhänen K, Myllynen P, Auriola S, Halonen T, Vähäkangas K (2011) Acute effects of ethanol on the transfer of nicotine and two dietary carcinogens in human placental perfusion. Toxicol Lett 205:257–264