Transport of Persistent Organic Pollutants across the human placenta

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Abstract

Prenatal life is the most sensitive stage of human development to environmental pollutants. Early exposure to Persistent Organic Pollutants (POPs) may increase the risk of adverse health effects during childhood. The mechanisms of transference of POPs during pregnancy are still not well understood. The present study is aimed to investigate the transfer of POPs between mother and fetus. The concentrations of 14 organochlorine pesticides, 7 polychlorinated biphenyls (PCBs) and 14 polybromodiphenyl ethers (PBDEs) congeners have been measured in 308 maternal serum samples, their respective umbilical cords and 50 placental tissues from a mother-infant cohort representative of Spanish general population. In general, the adjusted lipid-basis concentrations were higher in maternal serum than in cord serum and placenta. The concentrations of most pollutants between maternal serum and cord serum and between maternal serum and placenta were significantly correlated. These distributions were consistent with a predominant maternal source that transfers the pollutants into the placenta and the fetus. However, this distribution did not correspond to passive diffusion of these compounds between these tissues according to lipid content. The compounds more readily metabolized were higher in newborns, which suggest that differences in metabolic capabilities may be responsible of the observed variations in POP distributions between mother and newborns. Prenatal exposure to 4,4'-DDT and some PBDEs such as BDE 99 and BDE 209 is much higher than it could be anticipated from the composition of venous maternal blood. POP exposure assessment studies of newborns may overlook the effects of some of these pollutants if they only consider maternal determinations.

Highlights

1. The concentrations of most POPs in maternal and cord serum are correlated
2. A predominant mother-to-fetus pollutant transfer is observed
3. Pollutant transfer does not respond to passive lipid-associated diffusion
4. Immature fetal metabolism leads to higher POP accumulation
5. The degradable PBDEs are in higher concentrations in fetal than maternal serum

Keywords: Prenatal exposure, transplacental transfer, maternal serum, umbilical cord serum, placenta, DDT, DDE, hexachlorobenzene, hexachlorocyclohexane, PCBs, PBDEs.

Abbreviations:

BDE: bromodiphenyl ether

BMI: Body mass Index

CB: Chlorobiphenyl

HCB: Hexachlorobenzene

HCH: Hexachlorocyclohexane

GC-ECD: Gas chromatography coupled to electron capture detection

GC-MS: Gas chromatography coupled to mass spectrometry

INMA: Spanish Children´s Health and Environment

IQR: Interquartile range

LOD: Limit of detection

ng/g: Nanogram per gram

ng/mL: Nanogram per mililiter

NICI: Negative Ionization Chemical Ionization

OC: Organochlorine Compound

OCP: Organochlorine Pesticide

PBDE: Polybromodiphenyl ether

PCB: Polychlorobiphenyl

POP: Persistent Organic Pollutant

P : Percentile

SD: Standard deviation

1. Introduction

Human exposure to Persistent Organic Pollutants (POPs) begins in the uterine life period by transplacental transfer (Rogan et al. 1986). Placenta may prevent transfer of some pollutants but there is evidence that POPs, even those of high molecular weight can reach the fetuses (Vizcaino et al. 2011). Transfer of contaminants during pregnancy may have implications for fetus health. Fetuses are more vulnerable than adults to chemical exposure as their immune system and detoxification mechanisms are not fully developed. In-utero exposure may lead to severe repercussions for newborns and may predispose to late adult deleterious effects (Boekelheide et al. 2012). Thus, in utero exposure to POPs, including polybromodiphenyl ethers (PBDEs), polychlorobiphenyls (PCBs) and organochlorine pesticides (OCPs), has shown to increase the risk of adverse development outcomes in children (Gascon et al. 2012; Herbstman et al. 2010; Lopez-Espinosa et al. 2011; Park et al. 2008a; Ribas-Fito et al. 2007; Valvi et al. 2012). These results have increased notably the interest of the scientific community on exposure to these compounds during gestation.

Consequently, the number of studies reporting prenatal concentrations of POPs has increased in the recent years. Examination of this previous work evidences difficulties for comparison since there is a lack of standardization regarding subject selection, timing of sampling and reported levels (Jakobsson et al. 2012). Placenta, maternal and cord serum are the most common matrices to assess prenatal exposure to POPs, notwithstanding the processes of transfer of these pollutants from mother to fetus during pregnancy are still not clear (Barr et al. 2005). Previous studies stated that the distribution in body compartments of chemicals with log Kow >4 is driven solely by lipid fraction in tissues and blood (Haddad et al. 2000). Accordingly, partition ratios between matrices of POPs should be close to 1 when adjusted for lipid content.

However, there is small experimental evidence from human studies to evaluate this statement. Some exposure assessment studies have shown good correlations between mother, placenta and cord serum (Bergonzi et al. 2009) but studies describing the distributions and partition ratios of POPs between placenta, cord and maternal serum in humans are very scarce and limited to a reduced number of subjects (Needham et al. 2011) .

The present study is aimed to give insight into the transfer of POPs through placenta in a population exposed to baseline levels by examination of maternal and fetal distribution of POPs in mother-child pairs and quantification of the partition ratios between placenta, maternal and cord serum samples. Hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH), 44'-DDT and their principal metabolite 4,4'-DDE, PCBs (PCB 118, 138, 153 and 180) and PBDEs (BDE 28, 47, 99, 153, 154 and 209) have been studied. A mother-infant cohort from Asturias (Spain) that is representative of Spanish general population has been selected as test case. Except BDE 209 all these compounds are listed in the Stockholm Convention on POPs as priority chemicals. BDE 209 has been restricted in Europe but as its production and use is still ongoing in most of the world (EBFRIP, 2009) continued environmental exposure to this compound is expected over next years.

2. Material and Methods

2.1 Study Population

The cohort of study was established in Asturias by the Preventive Department of the University of Oviedo, as part of the INMA –Infancia y Medio Ambiente (Environment and Childhood) Project. This project encompasses seven Spanish areas and analyzes the influence of prenatal environmental exposures on growth, development, and health of infants from early fetal life until

childhood (Guxens et al. 2012). 494 pregnant women were recruited between May 2004 and June 2007. Deliveries took place between October 2004 and February 2008 at the reference hospital San Agustin, in Avilés (Asturias, Spain). 326 cord blood samples were successfully collected from assistance to 485 childbirths within the cohort population. 308 mother-umbilical cord blood paired samples were finally available as consequence of this project. Placental tissues were collected in a subset of 50 women. We present data of POP concentration for the 308 paired samples available and 50 placenta samples. The characteristics of the mothers from this group of 308 paired samples did not show significant differences from the whole recruited group (data not shown). The study protocol was approved by the Ethics Committee of the reference hospital, and informed consent was obtained for every participant.

2.2 Data and sample collection

Maternal blood samples were collected during the first trimester of gestation (median = 12 weeks; range = 10-13 wks).Whole cord blood samples were collected using venipuncture of cord vessels before the placenta was delivered. Maternal and cord serum were collected after centrifugation for 10 minutes, separated into aliquotes of 1 ml and stored at −80°C until analyses. The whole placenta was collected immediately after delivery. Half of the placenta, including maternal and fetal sides and central and peripheral parts, was placed in a glass container of a mixer (Büchi Mixer B-400 Büchi Laboratories AG, Flawil, Switzerland) for its homogenization. Once homogenized, aliquots of 25 g were stored and frozen at −80ºC. Pregnant women completed two detailed in-person questionnaires (weeks 10–13 and 28–32) on anthropometric and sociodemographic characteristics and lifestyle variables.

150 **2.3 Laboratory analyses**

151 The laboratory analytical methods and quality control procedures for the analysis of POPs have
152 been described elsewhere (Grimalt et al. 2010; Vizcaino et al. 2009). Concentrations of 7 PCB
153 congeners (PCB28, PCB52, PCB101, PCB118, PCB153, PCB138 and PCB180), α-HCH, β-
154 HCH, γ-HCH, δ-HCH, HCB, PeCB, 2,4'-DDT, 4,4'-DDT, 2,4'-DDE, 4,4'-DDE, 2,4'-DDD,
155 4,4'-DDD and 14 PBDE congeners (BDE17, BDE28, BDE47, BDE66, BDE71, BDE85,
156 BDE99, BDE 100, BDE153, BDE154 BDE138 BDE 183 and BDE 190 and BDE 209) were
157 analyzed in placental, maternal and cord serum samples.

158 Briefly, 1 mL of serum or 1 gr of placental tissue were spiked with the surrogate
159 standards tetrabromobenzene (TBB) and decachlorobiphenyl (CB 209) and vortex stirred for 30 s
160 at 2,000 rpm. n-Hexane (3 mL) was added, followed by concentrated sulfuric acid (2 mL). After
161 reaction, the mixture was stirred for 30 s and the supernatant n-hexane phase was separated by
162 centrifugation. The remaining sulfuric acid solution was re-extracted twice with 2 mL of n-
163 hexane (each by 30 s stirring and centrifugation). The combined n-hexane extracts (7 mL) were
164 additionally cleaned with sulfuric acid (2 mL, stirring 30 s). Then, the n-hexane phase was
165 separated by centrifugation and reduced to a small volume under a gentle nitrogen stream. The
166 extract was transferred to gas chromatography (GC) vials using four 25 μl rinses of isooctane.
167 CB 142, BDE 118 (20 μl) and [^{13}C]-BDE 209 (10 μl) were added as internal standards before
168 injection. Organochlorine compounds (OCs) were determined by GC with electron capture
169 detection (GC-ECD). BDE congeners were analyzed by GC coupled to mass spectrometry in
170 chemical ionization mode and negative ion recording.

171 Total cholesterol and triglycerides were determined in maternal and cord serum samples using
172 colorimetric enzymatic methods in the General Biochemistry Laboratory of Hospital San

Agustin. The samples were processed using a Roche Diagnostics COBAS C711. Total serum lipids concentrations were calculated as described by Phillips et al (1989) using the following formula:

$$TL = (2.27*TC) + TG + 62.3 \text{ mg·dL-1}$$

Placental lipids were determined gravimetrically. 1 gr of placental tissue was homogenized in 5 ml of chloroform:methanol:hydrochloric acid (20:10:0.1) (v/v/v). After repeating the process, 10 ml of 0.1 N HCl were added and centrifuged at 3000 rpm for10 min. The organic phase was then collected; the non-organic phase was re-extracted and added to the first extraction product. Total lipid content was determined after drying the organic extracts under a nitrogen stream to constant weight and total lipid were expressed in grams of lipid per gram of placenta (Lopez-Espinosa et al. 2007).

Validation of analytical results (including POPs and total lipid concentrations) was made by analysis of reference material obtained from the Artic Monitoring and Assessment Program (AMAP). We participate regularly in the AMAP Ring Test Proficiency Program for POPs in human serum (Centre de Toxicologie Institut National de Santé Publique du Québec, Québec, Canada) and the laboratory results usually are within 20% of the consensus values, including lipid concentrations.

2.4. Data analysis

POP levels were expressed in ng/mL. They were also adjusted to total serum lipid concentrations (ng/g lipid). Values of half detection limit were assigned when measurable analyte concentrations were not found. Spearman correlation and scatter plots were used to examine associations

between POP levels in placenta, maternal and cord serum. Placental transfer was evaluated by calculation of the concentrations ratios between paired samples for each compound on ng/mL and ng/g lipid:

$$R_{cm} = ; \quad R_{pm} =$$

where C_{uc} is the umbilical cord concentration, C_m is the maternal concentration and C_p is the placental concentration. Correlations and concentration ratios were calculated excluding non detected values. Values exceeding three times the standard deviation of the mean were considered outliers and consequently excluded from the ratio calculations. The ratios of each compound were only calculated if there were at least 10 paired samples above the detection limit (Needham, et al. 2011). Regression analyses with forcing regression to 0 were also calculated. No major differences were found between these options (data non shown). Therefore, only median concentration ratios are reported.

3. Results

Mean maternal age and standard deviation at delivery was 31.5 (4.3) (Table 1). 97.4% of the mothers were originally born in Spain, 63.5 % were primiparous and around 54% belonged to the lowest socioeconomic status. More than 42% had finished secondary education and about 76% were employed during pregnancy. 21.5% of the mothers were overweight and 6.8% were obese according to WHO body mass index (BMI) standards. On average, gestational weight gain was 14.1 ± 5.2 kg (Table 1).

The mean lipid content in placenta was 1.2% (range 0.43-1.7%) and total lipids in cord and maternal serum were 2.6 g/L (1.7-16 g/L) and 5.3 g/L (3.3-11 g/L), respectively.

PCB congeners 52 and 101, PBDE congeners 17, 66, 71, 85, 100, 138, 183 and 190 and PeCB, γ-HCH, δ-HCH, α-HCH, 2,4'-DDT, 2,4'-DDE, 4,4'-DDD and 2,4'-DDD were usually below limit of detection. The concentrations of POPs quantifiable in more than 50% of the samples in at least one of the studied matrices are shown in Table 2. 4,4'-DDE was the pesticide found in highest abundance and was found above limit of quantification in 100% of all samples analyzed. HCB was also above limit of quantification in 100% of the maternal serum and placenta samples and in 98% of the cord serum samples.

On lipid basis, the concentrations of organochlorine pesticides (OCPs) were higher in mothers than in newborns and placental samples (Table 2). 4,4'-DDT was the only exception to this trend and was higher in newborns. PCBs were found above limit of detection in all maternal samples. The maternal concentrations of these compounds (median=164 ng/g lipid and range between 47-1353 ng/g lipid) were much higher than in newborns (median=118 ng/g lipid and range between 24-967 ng/g lipid) and placenta (median=40 ng/g lipid and range between10-230 ng/g lipid). In all matrices, the PCB distributions were dominated by PCB 153, followed in abundance by PCB 180 and PCB 138 in newborns and mothers. In placenta, PCB 153 was followed by PCB 138 and PCB 28. The median concentrations of total PBDEs were higher in maternal serum (11 ng/g lipid) than in newborns (5.4 ng/g lipid) and placenta (2.3 ng/g lipid) (Table 2).

Different PBDE congener profiles were found in each of these three types of matrices. BDE 153 and 154 were most abundant congeners in maternal serum. In placenta the dominant congener was BDE 209. The median values of all congeners in cord blood serum were below detection limit but BDE47 was the compound found at higher concentrations in some samples (Table 2).

240 Spearman correlations between paired samples ranged from weakly negative to strongly
241 positive (Spearman rho= -0.04 to 0.9; Table 3). HCB and β-HCH showed significant correlations
242 between maternal and cord serum and placenta ($p < 0.001$). 4,4'-DDE also showed significant
243 correlations between these matrices. The concentrations of 4,4'-DDT in maternal and cord serum
244 were significantly correlated but those between maternal serum and placenta were not (Table 4).
245 The more chlorinated PCB congeners, PCBs 138, 153 and 180, were again showing significant
246 correlations between maternal serum, cord serum and placenta. The concentrations of the less
247 chlorinated congeners did not exhibit significant correlations. No correlation was observed for
248 the concentrations of PBDEs between maternal serum and placenta. However, statistically
249 significant correlations were observed for BDEs 47, 153 and 154 between maternal and cord
250 serum (Table 3). No substantial correlation differences were observed when considering the
251 concentrations on wet weight or lipid weight basis (data not shown).
252 Median C_{uc}/C_m varied between 0.28 and 0.91 when the concentrations were considered in
253 ng/mL and between 0.57 and 1.8 when calculating the concentrations in ng/g lipid (Table 4). The
254 PCB congeners showed different ratios following a trend that was consistent with the number of
255 chlorine substituents. CB 118 (5 chlorine substituents) had the highest ratio, 0.45, CB138 and
256 CB153 (6 chlorine substituents) had ratios of 0.39 and 0.37, respectively, and CB180 (7 chlorine
257 atoms) had a median ratio of 0.28. 4,4'-DDT showed the highest ratio, 0.91, of all studied
258 compounds. Among PBDEs, BDE 209 showed the highest ratio, 0.8, followed by BDE 99, 0.66,
259 and BDE 47, 0.58.
260 Median C_p/C_m varied between 0.36 and 1.2 in ng/mL and between 0.17 and 0.61 in ng/g
261 lipid. β-HCH presented the highest accumulation in placenta (C_p/C_m of 1.2 in ng/mL and 0.61 in
262 ng/ g lipid) and 4,4'-DDE the lowest (C_p/C_m of 0.36 in ng/mL and 0.17 in ng/ g lipid).

Another way to represent the distribution of these pollutants among the three matrices may be obtained by calculation of the relative percent distribution of the concentrations between maternal and cord samples (Fig. 1) or maternal, placental and cord samples (Fig. 2). These relative distributions must be calculated for each individual and the resulting proportions averaged. Obviously, only the individuals having concentration above quantification limits for all matrices considered were included in the compound averages. The distributions can also be calculated using either concentrations in ng L^{-1} or ng/g lipid. As observed for the ratios in the second case, the proportions of pollutants in cord serum or placenta increased (Figs. 1 and 2) because maternal serum has higher lipid content than cord serum and placenta, 5.3, 2.6 and 1.2 g L^{-1}, respectively.

4. Discussion

Correspondences in the composition of POPs in maternal and fetal serum and placenta

The maternal and newborn concentrations of the examined pollutants and their relative distributions differed slightly but the observed concentrations were highly correlated for most compounds. Thus, HCB, β-HCH, 4,4'-DDT, 4,4'-DDE, PCB 138, PCB 153, PCB 180, BDE 47, BDE 153 and BDE 154 showed significant Spearman coefficients ($p < 0.001$; Table 3). These results are in agreement with previous observations in which strong maternal-faetal correlations for the concentrations of these pollutants were found (Bergonzi, et al. 2011; Eik Anda et al. 2007; Fukata, et al. 2005; Mazdai, et al. 2003; Meironyté Guvenius, et al. 2003; Waliszewski et al. 2000a) and others involving significant correlations with lower Spearman coefficients (Covaci, et al. 2002; Jarrell, et al. 2005; Kawashiro et al. 2008; Koopman-Esseboom, et al. 1994; Park, et al. 2008b). Studies in Slovakia (Park et al. 2008b), Catalonia (Sala et al. 2001) or Belgium

(Covaci, et al. 2002) found similar maternal-newborn rates of PCBs, about 20-30% of maternal concentrations in cord serum on ng/mL as in the present study. In Sweden (Meironyté Guvenius et al. 2003), Poland (Jaraczewska, et al. 2006), Faroe Islands (Needham, et al. 2011) and Canada (Muckle, et al. 2001) lipid adjusted concentrations of cord serum ranged from 50 to 90% of maternal concentrations which is again in agreement with the present results.

Conversely, these correlations were not found in other studies (Antignac, et al. 2009; Gómara, et al. 2007; Kanja et al. 1992; Nair et al. 1996; Sala, et al. 2001; Soechitram, et al. 2004) and in some cases, e.g. Japan (Fukata et al. 2005) or Netherlands (Soechitram et al. 2004), lipid adjusted concentrations of PCBs were almost equal or slightly higher in cord than in maternal serum.

The correlations observed in the present study were found between maternal venous blood collected at 12 weeks of pregnancy and cord blood collected at delivery. In general, no changes in maternal POP concentrations have been observed during gestation (Glynn et al. 2011; Jarrell et al. 2005; Longnecker et al. 1999; Meijer et al. 2008) although some studies show discrepant results (Bloom et al. 2009; Bloom et al. 2007; Hansen et al. 2010).

Mother- to-fetus POPs transfer

The correlations observed in the present study involve a direct correspondence between higher maternal and newborn concentrations which is consistent with the transfer of pollutants from mother to fetus. Accordingly, all compounds exhibiting significant correlation coefficients between these two matrices have C_{uc}/C_m ratios < 1 when calculated from ng/mL units or, with the only exception of 4,4'-DDT, when calculated from ng/g lipid units (Table 4). Representation of the averaged relative proportion distributions of these pollutants in the maternal newborn serum pairs also show higher proportion of all correlated pollutants in the former than in the latter when

calculated over the ng/mL data as well as over ng/g lipid, with the only exception of 4,4'-DDT in this last case (Fig. 1).

Similarly, a high number of significant Spearman coefficients were observed between maternal and placental concentrations, e.g. HCB, β-HCH, 4,4'-DDE, PCB 138, PCB 153 and PCB 180 ($p < 0.001$). Again, these coefficients document a significant association between higher concentrations of pollutants in maternal serum and placenta which is again consistent with a transfer from the former to the second. Accordingly, the C_p/C_m ratios of the compounds exhibiting significant correlations between these two matrices are < 1 when calculated over ng/mL (with the only exception of β-HCH) or over ng/g lipid (Table 4) and the averaged distributions of these compounds between maternal and newborn serum and placenta show higher relative proportions of these correlated pollutants in maternal serum than in placenta in all cases except β-HCH when calculated over ng/mL. However, in these maternal-placental correlations 4,4'-DDT and none of the PBDEs show significant coefficients which constitutes a distinct feature from the results of the maternal-fetal concentrations.

Passive diffusion might control the transport of POPs across membranes (Myllynen et al. 2005) if the concentrations of these compounds tend to distribute uniformly among lipid-rich tissues (Russell et al. 1999; Waliszewski et al. 2001). In the present study, the concentration ratios between cord serum and maternal serum or placenta and maternal serum are not close to 1 when lipid adjusted (Table 4) which indicates that other processes also influence the distribution of these compounds among the different tissues.

Pollutant properties such as molecular weight, lipid solubility and protein binding (Myllynen et al. 2009) could also determine the transfer of pollutants from mother to fetus to a great extent (Needham et al. 2011). However, statistical analysis did not show any correlation

between these concentration ratios and chemical properties of these pollutants such as molecular weight, molar volume, number of halogen substituents or log octanol water partition coefficient (K_{ow}) (data non shown).

These results suggest that other processes besides transfer related to physical-chemical equilibrium are significant for the distribution of these pollutants between mother, placenta and fetus.

Selective accumulation in cord blood serum or placenta

β-HCH was the only compound which displayed higher concentrations in placenta than in cord serum (Fig. 2) suggesting that this membrane may act as a partial barrier for this contaminant. The PCB distributions in maternal and cord blood serum and in placenta were quite similar. Some previous studies reported decreases of the relative concentrations of the high chlorinated PCBs in cord serum (Koopman-Esseboom et al. 1994; Soechitram, et al. 2004) which are not observed in this study nor in other cohort studies (Carrizo et al., 2006; Vizcaino et al., 2010). Similarly, in some previous studies PCB distributions dominated by the less chlorinated congeners were reported in placenta (Fernandez et al. 2012; Gómara et al. 2012; Ma et al. 2012; Needham, et al. 2011) and this is not observed in the present study.

In this study, the significant correlations observed between PCBs in maternal serum and placenta and cord serum showed the highest Spearman coefficients among the congeners of higher chlorination (Table 3). These strong correlations require a uniform distribution of PCBs between the three types of matrices as observed in Table 2.

Conversely, the concentrations of the PCB congeners of lower degree of chlorination did not exhibit significant correlations between the three types of samples. These congeners are less hydrophobic and more difficult to accumulate in human tissues. The observed distributions show

concentrations above limit of quantification for all congeners in maternal serum and below limit of detection for PCB 118 in cord serum and PCB 28 in cord serum and placenta. The significant correlations of the concentrations of the higher chlorinated PCBs in all three matrices and their higher abundance in the maternal serum are consistent with the above mentioned distribution involving a maternal source that transfers these pollutants to the placenta and the fetal cord blood. However, this transfer is not a passive process related to diffusion into the lipid materials present in these tissues. Normalization to lipid content does not reflect similar values between these three sample matrices. Some active mechanisms such as the transport of enzymes through the membranes are likely associated to this transplacental transfer. These mechanisms may explain that compounds such as BDE 209 accumulate in cord blood.

However, some compounds exhibit specific trends. The C_{uc}/C_m ratios of 4,4'-DDT are higher than those of the other OCs. The higher 4,4'-DDT concentrations in newborns may result from a more rapid transformation to more stable metabolites such as 4,4'-DDE in mothers than fetus. The latter do not have efficient elimination mechanisms of toxicants (Alcorn and McNamara 2003), once pollutants cross the placenta they do not have the same capacity for metabolizing these compounds than their mothers. High concentrations of 4,4'-DDT in cord blood serum in relation to other OCs have also been observed in other studies (Al-Saleh et al. 2012; Muckle et al. 2001; Pathak et al. 2008; Waliszewski et al. 2000b)

Decreasing trends between maternal and fetal PBDE concentration ratios at higher degree of bromination have been reported in some studies (Frederiksen et al. 2009; Jakobsson, et al. 2012; Meironyté Guvenius, et al. 2003) in which it was concluded that the higher brominated congeners of these mixtures had more difficulties to cross the placenta. However, none of these studies analyzed BDE 209 or had sufficiently low detection limits to detect this compound in

cord blood serum. In the present study, we have observed higher concentration of BDE 209 in newborns than in their mothers which is in accordance to other studies (Antignac et al. 2009; Gómara et al. 2007) which reported an enrichment of BDE209 in cord serum. The presence of BDE209 in cord serum and placenta indicates its bioavailability and transport across placenta despite its size. In principle, small molecules penetrate membranes more easily than large ones (Arnot et al. 2010). However, once large molecules penetrate placenta and reach the fetus it might be more difficult to eliminate them due to the lower biotransformation capabilities of early life metabolism (Alcorn and McNamara 2003). BDE 209 was not very frequent in newborns, but whenever it was found it was the dominant PBDE congeners.

Similarly, higher C_{uc}/C_m ratios have been found for BDE 99 than for BDE 47. These results can be explained by differences in metabolic transformation between congeners. BDE 99 is usually metabolized to a greater extent than BDE 47 in adults (Stapleton et al. 2009). Previous studies have found high concentrations of BDE 99 in cord blood (Antignac, et al. 2009; Gómara, et al. 2007; Kim et al. 2012; Mazdai et al. 2003). Similarly, the high prevalence of BDE 154 in mothers compared to newborns indicates the difference of metabolic capacities of mothers and fetus. Higher presence of BDE 154 reflects biotransformation of more brominated congeners such as BDE 183 (Roberts et al. 2011).

Conclusions

The distributions of most OCs between maternal serum and cord serum and maternal serum and placenta are significantly correlated. In general, the highest relative concentrations are found in maternal serum and the lowest in cord serum. These distributions are consistent with a predominant maternal source that transfers the pollutants to the placenta and the fetus. However,

these distributions do not correspond to pollutant passive diffusion among the three types of tissues according to their lipid content. Conversely, they require an active transplacental transfer of the compounds possibly in association to the transport of enzymes through the membranes.

The compounds that can be metabolically transformed, namely 4,4'-DDT and several PBDEs, have been observed to accumulate selectively in cord blood. Once these are able to reach the fetus they are better preserved than in the maternal tissues. This difference evidences a low capacity of fetal metabolism for the degradation of organic pollutants which may lead to the accumulation of pollutants that usually are found in minor concentrations in adults or in mothers. POP exposure assessment studies of newborns may overlook the effects of some of these pollutants if they only consider maternal determinations.

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Figure captions

Fig. 1. Average percentage distribution of Persistent Organic Pollutants (POPs) between maternal and fetal serum expressed as ng/ml (a) and lipid adjusted concentrations (b) Interval bars correspond to 95% confidence interval.

Fig. 2. Average percentage distribution of Persistent Organic Pollutants (POPs) between maternal serum, placenta and fetal serum expressed as ng/ml (a) and lipid adjusted concentrations (b). Interval bars correspond to 95% confidence interval.