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POLYBROMINATED DIPHENYL ETHERS IN MATERNAL AND FETAL BLOOD SAMPLES

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Introduction

The aim of our study was to determine the human fetal and maternal serum concentrations of PBDEs in central Indiana. Although based on only a small sample set, our findings indicate that women in Indiana are exposed to levels even higher than those which were considered a reason for banning the use of PBDEs in products sold in Sweden. This preliminary report indicates that further, large-scale studies will be needed to assess exposure levels across a broader population, to identify the sources of exposure in the U.S. and to examine possible neurodevelopment deficits associated with high levels of exposure during fetal development.

Material and Methods

Clinical Materials. Institutional Review Board approval was obtained for studies involving humans. Patients, who were greater than 18 years of age, presenting in labor to Indiana University and Wishard Memorial County hospital in Indianapolis during August – December 2001 were asked to participate. Pregnancies were full term and no other major medical problems were noted in the mothers. Patients were asked to fill out a survey to determine: age, race, smoking habits, potential occupational exposures to PBDEs, e.g. working in computer or electronics manufacturing, repair or dismantling plants, and any other chemical exposures. Body mass index (BMI) (kg/m^2) was calculated from the patient's height and her pre-pregnancy weight and her weight at the time of delivery. Maternal blood was obtained when the patient was admitted to the labor and delivery suite, and fetal blood was obtained from the umbilical cord vein by syringe after delivery. The weight and presence of any congenital defects was noted for each baby.

Serum Extraction Procedure. The extraction of PBDEs from the serum was based on the method developed and validated by Hovander et al. (2002), but was modified to accommodate our larger sample sizes of 5-10 mL. After addition of internal standards and acidification, the samples were extracted with hexane/methyl *t*-butyl ether. An aliquot was removed for gravimetric determination of the lipid mass. The extracts were exchanged into hexane and reduced in volume to approximately 5 mL using a rotary evaporator. Lipids were removed by adding concentrated H_2SO_4. The samples were cleaned-up on water-deactivated silica gel and deactivated alumina columns. The sample was reduced in volume to approximately 20 μL under a stream of N_2 before injection into the gas chromatographic mass spectrometer.

Instrumental Analysis and Parameters. The samples were analyzed on an Agilent 6890 series gas chromatograph coupled to an Agilent 5973 mass spectrometer. A 60-m column was used to insure

separation of BDE-154 from polybrominated biphenyl 153. The mass spectrometer was operated in electron capture negative ionization mode (ECNI) using methane as the buffer gas. Selected ion monitoring (SIM) of the two bromide ions at m/z 79 and 81 was used to detect the PBDEs. The compounds were quantitated using quantitation standards with known amounts of all the target compounds, internal standards, and recovery standards. Normal QA/QC precautions were followed.

Results and Discussion

Twenty six paired maternal and fetal samples were analyzed for PBDE; six pairs of these samples are not reported because they did not meet quality control specifications due to problems with blank analysis. Of the 20 patients reported, none of the mothers reported any work-related potential for exposure to PBDEs. Six different congeners of PBDE were measured in the serum samples. Of the six congeners detected, BDE-47 accounted for the majority (40 – 79%) of all PBDEs; BDE-99 was the next most abundant congener at 8 – 33%. The concentrations of total PBDEs found in maternal sera ranged from 5 – 580 ng/g lipid (average = 86 ng/g lipid), and the concentrations found in fetal sera ranged from 13 – 460 ng/g lipid (average = 75 ng/g lipid); see the figure. The PBDE concentrations were highly correlated between mother and fetal blood (r^2 = 0.971) and exhibited no statistical differences between maternal and fetal blood pairs.

There was no apparent correlation between concentrations of PBDEs and any of the clinical parameters. Serum PBDE concentrations did not vary according to age or BMI. Nor was there any relationship between infant birth weight and PBDE concentrations. Thyroid hormones were assayed in nine of the twenty sample pairs. There was no apparent correlation between total PBDEs and T_3 or T_4 concentrations (total or free).

This is the first report of PBDE blood levels in pregnant women and their fetuses from the U.S. When compared to the average levels in a similar population of Swedish mothers and newborns (Guvenius et al, 2003), the average serum PBDE levels in our study were 21-fold higher for maternal blood and 22-fold higher for fetal blood. (This comparison excludes two pairs from our study with unusually high concentrations between 350 – 580 ng/g lipid). Likewise, the range of BDE-47 levels we report in women from Indiana was approximately 20-fold that found in Norwegian blood samples from 1997-1999 (Thomsen et al. 2002). Moreover, the median blood levels found in our population indicate an exposure to PBDEs comparable to that of Swedish workers considered to have had direct, work-related exposures (Jakobsson et al. 2002; Sjodin et al. 1999). In contrast, samples collected from adult US blood donors in 1988 had sum concentrations of PBDEs that were much lower (ca. 0.12 - 0.65 ng/g lipid) (Sjodin et al. 2001) than the levels we found in the maternal samples. The reason for the disparity between our results and those of previous studies is not positively known, however, because PBDEs are not manufactured in Europe, as they are in the U.S. (Darnerud et al. 2001), exposure levels may be lower in Europe. In addition, concentrations of PBDEs in the North American environment have increased since 1988 (Ikonomou et al. 2002; Norstrom et al. 2002). It will require further investigation to determine if the high human concentrations reported here represents a regional or a national trend. However, in a review of the currently available data, Ryan observed that concentrations of PBDEs in breast milk of North American women were 40 - 50 times greater than concentrations previously described in Swedish breast milk samples (Betts 2002). Similarly, a recent study of PBDEs in breast fat of women in San Francisco found concentrations averaging 86 ng/g lipid (She et al. 2002). Together

with our study, these observations indicate that women in North America are exposed to much higher levels of PBDEs than are Europeans.

In general, the PBDE congener profile we found in human serum was similar to that detected in environmental samples, with the exception that there is an apparent decrease in the proportion of BDE-99. In air, BDE-99 accounts for 35% of the total PBDEs (Strandberg et al. 2001), while in fish it was 27% (Dodder et al. 2002), and in the humans in this study it was 15% and 18% for the maternal and cord samples, respectively. This range for BDE-99 is similar to the range found in other human studies (Sjodin et al. 2001; Hovander et al. 2002). The lower proportion of BDE-99 may indicate a differential metabolic degradation of BDE-99 as it goes through the food chain. In addition, BDE-183 was detected in only 7 of the 40 samples, even though it is the primary congener in the "Octa-BDE" technical mixture (Darnerud et al. 2001). This may be because BDE-183, like BDE-209, has a lower bioavailability compared to the other lower brominated congeners or because its low vapor pressure does not facilitate its atmospheric transport as readily as the other congeners (Dodder et al 2002; Strandberg et al 2001). On the other hand, relatively high levels of BDE-183 have been observed in occupationally exposed workers (Sjodin et al. 1999; Thomsen et al. 2001).

It is apparent that, like PCBs and organochlorine pesticides (DeKoning and Karmaus 2000; Covaci et al. 2002; Sala et al. 2001; Waliszewski et al. 2000), PBDEs cross the placenta into the fetal circulation. Furthermore, our results indicate that all tetra through hepta substituted congeners have approximately the same potential to cross the placenta. The high correlation between maternal and fetal blood levels of PBDE indicates that measurement of maternal PBDE yields a strong indication of PBDE exposure of the fetus at the time of birth; whether this true at earlier points in gestation will require additional studies. It is likely that lipophilic compounds such as PBDEs move into fetal circulation along with maternal lipids. Experimental analysis of maternal and fetal blood samples and lipid infusion studies indicate that there is an influx of lipids from maternal and placental sources into the fetal circulation (Elphick et al. 1978; Hendrickse et al. 1985; Berghaus et al. 1998). Furthermore, there is a dramatic mobilization of maternal fat stores during the third trimester of gestation (Pipe et al. 1979), a period critical to brain development (Porterfield 2000), and possibly the biological significance and bioavailability of PBDEs.

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