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# The human body burden of polybrominated diphenyl ethers and their relationships with thyroid hormones in the general population in Northern China

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## HIGHLIGHTS

- The PBDE level was lower than that in Southern China, Europe, and North America.
- BDE-209 was found as the dominant congener in 124 serum samples in Northern China.
- Even at low level, PBDEs may interfere with $T_3$ levels in the general population.

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## ABSTRACT

This study was conducted to determine the human body burden of polybrominated diphenyl ethers (PBDEs) and then clarify the relationships between that and the disruption of thyroid hormones in the general population in Northern China. Between November 2010 and May 2011, 124 serum samples were obtained from volunteers from the provinces of Shanxi and Liaoning. Serum samples were prepared by solid-phase extraction and analyzed for BDE-17, 28, 47, 66, 99, 100, 153, 154, 183 and 209 by gas chromatography–negative chemical ionization mass spectrometry. The median concentration of the total PBDEs was 7.2 ng/g lipid weights (lw); concentrations ranged from 2.1 to 160.3 ng/g lw. The PBDE profiles in this study differed from those of other general populations. BDE-209 was the most abundant congener (median, 5.0 ng/g lw; range, non-detected — 157.1 ng/g lw), accounting for more than 75% of the total PBDEs, followed by BDE-153. The total PBDE concentrations in men were significantly higher as compared to women. The donors' age was correlated with a few PBDE congeners, but was not correlated with the total PBDE concentrations. The overall level of PBDEs in this study was lower than that observed in general populations in Southern China, Europe, and North America. There were apparent correlations between concentrations of several PBDE congeners and thyroid hormones. Triiodothyronine ($T_3$) was correlated with BDE-99 and 209 and inversely correlated with BDE-17, 28, 47, 153, 183, and the summed tri- to hepta-PBDE congeners ($\sum_{3-7}$PBDEs). Thyroid-stimulating hormone (TSH) was correlated with BDE-17, 28, 47, and 183 and inversely correlated with BDE-99. No correlation between free tetraidothyronine ($FT_4$) and PBDEs was observed. Logistic regression analysis results indicated that those with higher levels of BDE-17 or BDE-153 had significantly lower odds of having $T_3$ levels above the normal range compared to those with lower levels of BDE-17 or BDE-153. Association between $FT_4$ and BDE-153 disappeared after controlling for sex and age. However, there was no significant association between TSH and PBDEs. The results of the present study showed that even at a relatively low level, PBDEs might interfere with the thyroid hormone levels in the general population.



## 1. Introduction

Polybrominated diphenyl ethers (PBDEs) are used as flame retardants in a wide variety of commercial and household products. PBDEs are not covalently bound to the polymer, but are additive flame retardants; therefore, they are more likely to leach from such products during their lifetime (Sjodin et al., 2003). PBDEs have been recognized

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as ubiquitous contaminants and have been found in the environment (Birgul et al., 2012; Wu et al., 2012), wild life (Desforges et al., 2012; Shaw et al., 2012) and humans (Fujii et al., 2012; Hedley et al., 2010; Kim et al., 2012; Miller et al., 2012; Schecter et al., 2010).

Due to their properties of lipophilicity, persistence, bioaccumulation, and susceptibility to long-range environmental transport, penta-BDEs and octa-BDEs were removed from the European (1998) and North American (2004) marketplace (Ross et al., 2009). Deca-BDEs, however, are still being manufactured on a large scale and used globally. At present, there is no restriction on the manufacture and use of penta-BDEs, octa-BDEs, and deca-BDEs in China. Deca-BDEs were the major products in China in all flame retardants. In 2004, the production of deca-BDEs was 25000 t (Chen, 2006).

The majority of studies on human body burdens of PBDEs have been conducted in North America (Johnson-Restrepo et al., 2007; Miller et al., 2012; Siddique et al., 2012), Europe (Covaci et al., 2008; Thomsen et al., 2002), and Japan (Akutsu et al., 2008; Fujii et al., 2012). Data on the human body burden of PBDEs in China, especially for the general population, remain scarce (Bi et al., 2006; Chen et al., 2010; Li et al., 2008).

In animal experiments, PBDEs have been shown to cause developmental neurotoxicity and endocrine disruption (Costa and Giordano, 2007; Darnerud, 2008). Adverse health effects of PBDE exposure, such as adverse neurodevelopment, association with congenital cryptorchidism, and association with behavioral factors have also been reported in humans (Buttke et al., 2012; Herbstman et al., 2010; Main et al., 2007).

As the structure of PBDEs and their metabolites (hydroxy- and methoxy-BDEs) are similar to thyroxine and triiodothyronine ($T_3$), i.e., they possess two halogenated phenyl rings attached by an ether link (McDonald, 2002), concerns have been raised regarding their effect on thyroid hormones (THs) function, such as binding to TH receptors and displacing THs (Thomas, 2010). In laboratory animal studies, PBDEs affected thyroid regulation by decreasing circulating levels of thyroid hormones, altering the expression of genes that encode thyroid-regulating proteins, and reducing the activity of thyroid-regulating enzymes (Marchesini et al., 2008). THs influence the function of nearly all tissues via their effects on cellular metabolism and the essential roles they play in differentiation and growth (Talsness et al., 2007). THs disruption is associated with many adverse health outcomes, including goiter, benign and neoplastic thyroid diseases, and neurodevelopmental toxicity (McDonald, 2002). In experimental animal studies, the PBDE-related alteration of TH levels was observed in rodents (Van der Ven et al., 2008), lambs (Abdelouahab et al., 2009), and fish and marine mammals (Ross et al., 2009). However, data on humans mostly focused on the general population from North America with high PBDE exposure levels (Chevrier et al., 2010; Mazdai et al., 2003; Turyk et al., 2008).

The purpose of this study was to examine the PBDE levels in serum samples from the general population in Northern China and explore the relationships between PBDEs and THs in humans. PBDE levels and congener-specific patterns were analyzed as functions of ages and sex.

## 2. Materials and methods

### 2.1. Study participants and biological samples

Blood samples were obtained from 124 volunteers (64 from Shanxi Province and 60 from Liaoning Province) in Northern China between November 2010 and May 2011. Questionnaires were designed to obtain information of participants, such as age, sex, job, years of working, heath status (if they had thyroid disease or under relevant treatment), etc. None of the participants had been occupationally exposed to PBDEs or involved in the manufacture of PBDE commercial products. No volunteer had thyroid disease or was currently under treatment for thyroid disease.

The volunteers (60 men and 64 women) were between 19 and 55 years old; the mean age of 33.4 years. The informed consents of all volunteers were obtained before enrollment. Medical professionals collected blood from the cubital vein in vacuum blood collection polypropylene tubes. The serum was separated by centrifugation (822.5 *g*) for 15 min and thereafter transferred to new polypropylene tubes. Frozen serum specimens were transported to the laboratory and stored at −20 °C until analysis.

### 2.2. Chemicals

Ten PBDE congeners were measured in the serum samples: BDE-17, 28, 47, 66, 100, 99, 154, 153, 183, and 209. Calibration standard solutions (BDE-17, 28, 47, 66, 100, 99, 154, 153, 183, and 209 in nonane) and isotope dilution internal standard solution ($^{13}$C-BDE-209 in nonane) were obtained from Wellington Laboratories (Guelph, Canada). Internal standard solution (BDE-77 in isooctane) was purchased from AccuStandard Inc. (New Haven, CT, USA). All solvents were of pesticide analysis grade and were obtained from J.T. Baker (Center Valley, PA, USA), except acetonitrile (Thermo Fisher Scientific; Waltham, MA, USA) and formic acid (96%, Dikma Technologies; Beijing, China). Sulphuric acid was of analytical grade (Beijing, China). Oasis® HLB custom-made solid-phase extraction (SPE) cartridges (60 mg/3 mL; the sorbent was copolymer polymerized with lipophilic divinylbenzene and hydrophilic N-vinyl-pyrrolidone) were purchased from Waters Corporation (Milford, MA, USA). The standard reference material (organic contaminants in fortified human serum) SRM 1958 was purchased from the National Institute of Standards and Technology (Gaithersburg, MD, USA).

### 2.3. Sample preparation

The sample preparation methodology has been described elsewhere (Huang et al., 2011). In brief, frozen serum samples were thawed and brought to ambient temperature. BDE-77 (50 pg) and $^{13}$C-BDE-209 (1 ng) were added to the serum sample (3 mL) as internal standards, vortex mixed, and kept in a refrigerator (4 °C) overnight to equilibrate. Formic acid and acetonitrile were used to denature serum proteins before the solid phase extraction (SPE) was carried out. The SPE columns were pre-washed with dichloromethane (DCM) and conditioned with water and methanol. After sample loading, the lipids were decomposed by treatment with concentrated sulphuric acid directly on the SPE columns. The SPE cartridges were eluted with DCM and the eluate was solvent-exchanged to hexane and concentrated for gas chromatography–mass spectrometry (GC–MS) analysis.

### 2.4. Instrumental analyses

The samples were analyzed on a Shimadzu QP2010-plus gas chromatography mass spectrometer (Shimadzu Corporation, Tokyo, Japan). The chromatographic separation for tri- to hepta-BDEs was carried out on a VF-5 ms capillary column (30 m × 0.25 mm internal diameter [i.d.], 0.25 μm film thickness). The column temperature program was initiated at 50 °C for 2 min, 45 °C/min to 200 °C, 10 °C/min to 320 °C, and held at 320 °C for 5 min. For BDE-209, a short column with a thin film (15 m × 0.25 mm i.d., 0.10 μm film thickness) was used to avoid its degradation during analysis. The GC oven temperature for BDE-209 was programmed as follows: 80 °C for 1 min, 30 °C/min to 280 °C, 15 °C/min to 310 °C, held for 1.5 min, 30 °C/min to 320 °C, and held at 320 °C for 3.5 min. The injection port was 280 °C. The ion source and interface were 250 °C and 300 °C, respectively.

The mass spectrometer was operated in negative chemical ionization mode using methane as the buffer gas. The isotope dilution method was applied for quantification of BDE-209, and the internal standard method for other PBDEs. Selected ion monitoring of the ions at *m/z* 79 and 81 was used to detect the PBDEs. The ions at *m/z* 486 and 488