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Geographical Distribution of Perfluorinated Compounds in Human Blood from Liaoning Province, China

JIAYING LIU,[†] JINGGUANG LI,*[,†] YAN LUAN,[‡] YUNFENG ZHAO,[†] AND YONGNING WU*[,†]

National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, 29, Nanwei Road, Beijing, 100050, China, Liaoning Provincial Blood Center, Shenyang, 110044, China

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Perfluorinated compounds (PFCs), such as perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA), have been identified widely in human. Monitoring of geographical distribution of PFCs in human blood can provide the information to better characterize the exposure source and pathway of these compounds. In this study, 13 PFCs were detected in 138 whole blood samples collected in 2008 from seven cities (Liaoning province, China) including Fuxin, Jinzhou, Shenyang, Anshan, Yingkou, Huludao, and Dalian. The highest geometric mean (GM) concentration of total PFCs was found in samples from Fuxin (17.27 ng/mL) followed by Shenyang (12.70 ng/mL) and Anshan (12.63 ng/mL). The composition profile of PFCs was varied in blood samples from seven cities. In Fuxin and Jinzhou, the percentage proportion of PFOA was significantly higher than that of perfluorohexanesulfonate (PFHxS) by about two times. By contrast, in Shenyang, Anshan, and Yingkou, the percentage proportion of PFHxS was about three times higher than that of PFOA. In Huludao and Dalian, the profile of PFCs in blood was very similar with comparable proportions of PFOA and PFHxS. The results suggested different human exposure sources and pathways of PFCs in Liaoning province, China.

Introduction

Perfluorinated compounds (PFCs) have been industrially produced for several decades. Perfluorosulfonic acids (PFSAs) and perfluoroalkylcarboxylic acids (PFCAs) are both lipophobic and hydrophobic and have strong surface-active property. The unique characteristic of these compounds makes them to be widely used in industrial and commercial products such as surfactants, lubricants, paints, polishes, fire-retarding, and food packaging (*1, 2*). In recent years, these compounds, referred to as "emerging persistent organic pollutants" (*3*), posed increasing concern for their nature of resistance to degradation in the environment (*4*), global distribution (*5*−*7*), environmental toxic effects and health risk to humans (*2, 8*−*11*).

An increasing number of studies have shown that humans are widely exposed to PFCs, and perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) are generally the most prevalent PFCs found in human (*10, 12*). In the U.S., PFCs serum concentrations increased between 1974 and 1989, and reached a plateau level at 1989 (*13*). The study on PFCs in American Red Cross blood donors suggested a decrease of these compounds after the year 2000, coinciding with the phase-out in PFOS production in the U.S. (*14*). The same declining trend was found by an exposure assessment using of newborn screening program blood spot between 1997 and 2007 (*15*) and the data from U.S. National Health and Nutrition Examination Survey (NHANES) in 1999−2000 and 2003−2004 (*16*). However, an increase of serum levels of PFOS and PFOA was found between 1977 and 2003 in Japan (*12*). The increasing trend of serum levels of PFOS and PFOA was also found from 1987 to 2002 in Shenyang, China (*17*). No temporal trend was clearly detected for PFOS from the analysis of composite samples of breast milk collected yearly in Sweden between 1996 and 2004 (*18*).

The exposure sources and pathways for general population have not been well-characterized. PFCs have been found in drinking water, household dust, indoor air, and food (*19*−*22*). Some studies showed that dietary intake seems to be an important source of exposure of general population to PFOS and PFOA (*22*). Drinking water might be a source of exposure to PFCs as important as the dietary intake of these pollutants (*23*). The results of a study from Germany showed that the PFCs concentration in blood plasma of children and adults exposed to PFCs through contaminated drinking water were increasd 4−8-fold as compared with controls (*24*). Human exposure of PFCs from water was also found in the U.S. (*25*). Furthermore, the biotransformation processes from some precursors, such as perfluoroalkyl sulfonamide alcohols and derivatives and fluorotelomer alcohols (FTOHs), to PFSAs and PFCAs, respectively, may be a potential human exposure source (*26*). For example, production of PFCAs from the biotransformation of FTOH-based polyfluoroalkyl phosphate surfactants that is applied to food contact paper packaging may be a significant source of PFCA contamination to the human population (*27*).

Analysis of human exposure to PFCs in different geographical areas can provide the information on sources or pathways of human exposure. In China, the result of a previous study showed that the PFCs profiles varied in the human blood samples from nine cities in China (*28*). It suggested that there might be different exposure sources or pathways of PFCs for general population in various regions of China. Among the cities, the highest level of PFCs was found in blood from Shenyang, the capital of Liaoning province. To our knowledge, one of the largest fluorochemical manufacture plants of China is located in Liaoning province, which may be a potential contaminant source of PFCs to the local environment and humans. The purpose of this study is to characterize the geographical distribution of PFCs in human blood collected from different regions in Liaoning province for better understanding the sources and pathways of human exposure to PFCs.

Materials and Methods

Samples Collection. As shown in Figure 1, seven cities of Fuxin (42°00N, 121°65E), Jinzhou (41°13N, 121°15E), Shenyang (41°80N, 123°38E), Anshan (41°12N, 122°85E), Yingkou (40°65N, 122°18E), Dalian (38°92N, 121°62E), and Huludao (40°56N, 120°38E) were selected for sampling.

Through collaboration with Liaoning Provincial Blood Center between March and September 2008, 138 human whole blood samples were obtained from donors aged 19−55

* Corresponding authors phone: +86-10-83132933; fax: +86-10-83132933; e-mail: lichrom@yahoo.com.cn. Y.W. phone: +86-10-67776790; fax: +86-10-67776790; e-mail: wuyncdc@yahoo.com.cn.
[†] Chinese Center for Disease Control and Prevention.
[‡] Liaoning Provincial Blood Center.

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FIGURE 1. Sampling locations in Liaoning province.

TABLE 1. Summary of the Demographic Information of Blood Samples

		Male		Female	
source of blood	age group	age: mean (range)	no. of samples	age: mean (range)	no. of samples
Fuxin	<30	20(20−21)	5	24(21−28)	5
	>40	45(40−50)	5	47(44−53)	5
Jinzhou	<30	23(20−27)	5	28(25−30)	5
	>40	50(48−52)	5	44(43−46)	5
Shenyang	<30	23(21−25)	5	21(20−23)	5
	>40	42(40−45)	5	44(40−45)	5
Anshan	<30	21(20−22)	5	23(19−26)	5
	>40	45(42−49)	5	42(40−46)	4
Yingkou	<30	24(20−29)	5	21(19−25)	5
	>40	44(41−45)	5	44(41−50)	5
Dalian	<30	22(20−24)	10	22(20−23)	10
	>40				
Huludao	<30	25(21−29)	5	26(20−30)	5
	>40	53(51−55)	5	44(41−48)	4
Total			70		68

from seven cities in Liaoning province. There were approximately 20 donors with a sex ratio of 1:1 in each city. Furthermore, each gender group was divided into two subgroups according to age of <30 and >40 except in Dalian where donors' age range was from 20 to 23. The demographic information including age, sex, and location are shown in Table 1. Whole blood samples were stored in polypropylene (PP) containers at −20° until analysis.

Reagents and Chemicals. The standard solutions containing perfluorobutanesufonate (PFBS), perfluorohexanesulfonate (PFHxS), perfluoroheptanesulfonate (PFHpS), perfluorooctanesulfonate (PFOS), perfluorodecanesulfonate (PFDS), perfluoropentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUdA), and perfluoroundecanoic acid (PFDoA) were purchased from Wellington Laboratories (Guelph, Canada). The internal standard of perfluoro-1-(1,2,3,4-$^{13}C_4$)octanesulfonate ($^{13}C_4$−PFOS) and perfluoro-n-(1,2,3,4-$^{13}C_4$)octanoic acid ($^{13}C_4$−PFOA) were also purchased from Wellington Laboratories. Methanol of high-performance liquid chromatography (HPLC) grade was purchased from J. T. Baker (Phillipsburg, NJ). Milli-Q water was used throughout the study. Tetra-*n*-butylammonium hydrogen sulfate (TBA) was purchased from Acros (Morris Plains, NJ), and methyl-tert-butyl ether (MTBE) was purchased from SIGMA-Aldrich (St. Louis, MO).

TABLE 2. Mass Transition, Limit of Detection (LOD) for Selected PFCs and Mean Recovery from Spiked Whole Blood

			mean recovery (%) (n = 5)	
compound	mass transition	LOD (ng/mL)	low level (10 ng/mL)	high level (30 ng/mL)
PFBS	299 → 80	0.010	58	61
PFHxS	399 → 80	0.012	87	94
PFHpS	449 → 80	0.019	95	99
PFOS	499 → 80	0.021	103	98
PFDS	599 → 80	0.034	74	82
PFPeA	263 → 219	0.014	51	63
PFHxA	313 → 269	0.009	98	97
PFHpA	363 → 319	0.013	81	95
PFOA	413 → 369	0.024	102	98
PFNA	463 → 419	0.013	74	91
PFDA	513 → 469	0.024	92	93
PFUdA	563 → 519	0.033	78	79
PFDoA	613 → 569	0.029	80	76

Extraction and Instrumental Analysis. The internal standards, $^{13}C_4$−PFOS and $^{13}C_4$−PFOA were added to each sample prior to extraction. The whole blood samples were extracted using the method developed by Hansen et al. (*29*). Briefly, 1 mL of whole blood, 1 mL of 0.5 M TBA solution and 2 mL of 0.25 M sodium carbonate buffer were mixed in a 15 mL prewashed polypropylene tube for extraction. Five milliliters of MTBE was added to the solution, the organic and aqueous layers were separated by centrifugation, and the organic layer was removed to another tube. The aqueous mixture was extracted thrice with MTBE. The organic extracting solvent was evaporated at ambient temperature under nitrogen gas flow, and then reconstituted in 1 mL of methanol/water (1:1). After centrifugation, the supernatant was passing through a 0.2 μL nylon filter (Sartorius, Goettingen, Germany) to remove particles.

PFCs were analyzed using ultra performance liquid chromatography with tandem mass spectrometry (UPLC-MS/MS). Separation of analytes was performed by a Waters Acquity UPLC system (Waters, Milford, MA) interfaced with a Quattro Premier mass spectrometer (Waters) operated in the electrospray negative mode. A 20 μL aliquot of the sample extract was injected with a full loop injection into a 2.1 × 50 mm BEH C18 column which was heated to 50° Two mM ammonium acetate aqueous solution and methanol were used as mobile phases. The flow rate was 0.4 mL/min. The triple-quadrupole mass spectrometer was operated with multiple-reaction-monitoring. The mass transition for each compound is listed in Table 2.

Quantification and Quality Assurance. Quantification was performed by relating the area of the analytes to the area of the isotope labeled internal standards ($^{13}C_4$−PFOS, $^{13}C_4$−PFOA). In consideration of matrix effect, calibration standards were matched with authentic sample extracts.

One blank sample (Milli-Q water) was extracted with each batch of 20 samples and methanol was injected before the sample sequence. No contamination of PFCs was found above limit of detection (LOD) in solution and reagents used in this analysis. The containers like tubes for blood collection were extracted with methanol and contained no PFCs above the LOD. The analysis system and the filters used in sample preparation were all washed by water and methanol before analyzing the sample. The LOD and mean extraction recoveries for thirteen PFCs were listed in Table 2. The LOD was defined as the concentration needed to produce a signal-to-noise ratio of 3:1 for measured PFCs. Matrix spike recovery

TABLE 3. The GM Concentrations of PFCs in Whole Blood Samples Stratified by Gender and Age (ng/mL)

	male		female	
	<30	>40	<30	>40
PFHxS	1.45	2.72	1.17	1.85
PFHpS	0.31	0.57	0.20	0.64
PFOS	5.70	7.71	4.10	6.67
PFOA	0.95	1.41	1.02	1.29
PFNA	0.38	0.77	0.44	0.68
PFDA	0.09	0.17	0.08	0.15
PFUdA	0.19	0.29	0.11	0.25

studies were carried out in two spike levels (10 ng/mL, 30 ng/mL) using rat blood. The repeated extractions were performed to evaluate the repeatability and reproducibility of the method. The intraday relative standard deviations (RSDs) ($n = 5$) of spiked whole blood samples were between 4 and 11%, and the interday RSDs ($n = 5$) over 3 weeks were between 6 and 28%.

Statistical Analysis. The Mann−Whitney test was used to assess the differences in concentrations of PFCs in blood samples between genders, two age groups. Undetectable concentration was accounted as a value equal to the LOD divided by the square root of 2 (*16, 30*). All the statistical analyses were performed by the software of SPSS 13.0.

Results and Discussion

Of the 13 PFCs analyzed, eight PFCs were found above the detection limit with varying frequency of detection in blood samples. High frequencies of detection were obtained from PFOS (100%), PFHxS (100%), PFOA (100%), PFNA (99%), PFHpS (91%), PFDA (88%), and PFUdA (79%). PFDS was only detected in 22% of the samples at concentrations near LOD. Therefore, this compound will not be discussed further. The highest geometric mean (GM) concentration for all samples was obtained for PFOS (5.58 ng/mL) with a range from 0.41 ng/mL to 33.71 ng/mL followed by PFHxS (1.47 ng/mL) with a range from 0.12 to 25.23 ng/mL and PFOA (1.01 ng/mL) with a range from 0.05 to 76.26 ng/mL. The lowest GM concentration for all samples was obtained for PFDA (0.10 ng/mL) with a range from <LOD to 0.70 ng/mL. The GM concentration of total PFCs including PFHxS, PFHpS, PFOS, PFOA, PFNA, PFDA, and PFUdA for 138 samples was 10.84 ng/mL with a range from 1.14 to 83.65 ng/mL. On average, the greatest contribution was from PFOS (57%) followed by PFHxS (16%) and PFOA (13%) while the individual percentage contribution of other four compounds was less than 5%.

Gender and Age. To investigate possible gender and age influence on blood PFCs level, data of blood samples were pooled and then analyzed according to gender and age respectively. The Table 3 showed the GM concentrations of PFCs in blood samples stratified by gender and age. The GM concentration of total PFCs was a little higher in males (11.66 ng/mL) than that in females (9.98 ng/mL). However, no statistic difference was found ($p = 0.09$). The similar result was obtained for each detectable PFC except for PFNA. The GM concentration of PFNA in blood of females (0.52 ng/mL) was marginally higher than that of males (0.50 ng/mL). The effect of age on blood PFCs levels was found with significantly higher level in high age people than in low age people ($p < 0.01$) for all PFCs except for PFOA ($p = 0.08$) in present study. The gender and age effects on PFCs in human blood were examined in different studies (*10, 16, 28, 31, 32*). For example, in a study of human blood from Spain, the blood levels of PFHxS and PFOA were significantly higher in men than in women, whereas PFHxS was higher in younger group subjects (*31*). In the U.S. NHANES, males had higher GM concentration of PFOS, PFOA, and PFHxS than did females, whereas the GM concentrations of PFOS, PFOA, and PFNA were quite similar among age groups (*16*). The inconsistent results of gender and age related effects of PFCs in human blood may be attributable to confounding factors, e.g., occupation, lifestyle, history of exposure, and some physiological factors (*32*).

TABLE 4. The GM Concentrations of PFCs in Whole Blood Samples from Seven Cities (ng/mL)

	PFHxS	PFHpS	PFOS	PFOA	PFNA	PFDA	PFUdA
Dalian	0.61	0.15	3.63	0.44	0.33	0.05	0.17
Huludao	0.78	0.26	5.13	0.57	0.52	0.10	0.56
Yingkou	2.76	0.52	6.38	0.74	0.69	0.09	0.13
Anshan	2.24	0.39	7.41	0.59	0.42	0.10	0.31
Shenyang	2.12	0.48	7.19	0.98	0.48	0.16	0.09
Jinzhou	1.50	0.29	4.28	2.45	0.60	0.12	0.19
Fuxin	1.57	0.43	6.42	3.81	0.59	0.13	0.19

Geographical Trends. The GM concentrations of PFCs in blood samples from seven cities were listed respectively in the Table 4. Generally, PFOS, PFHxS, and PFOA were prevalent PFCs in blood samples from each city. The highest GM concentration of PFOS was obtained from Anshan (7.41 ng/mL) followed by Shenyang (7.19 ng/mL) and Fuxin (6.42 ng/mL). The highest GM concentration of PFHxS was found in samples from Yingkou (2.76 ng/mL) followed by Anshan (2.24 ng/mL) and Shenyang (2.12 ng/mL). While the GM concentration of PFOA from Fuxin (3.81 ng/mL) and Jinzhou (2.45 ng/mL) was distinctly higher than that from other cities ranging from 0.44 to 0.98 ng/mL. Among seven cities, the highest GM concentration of total PFCs was found in Fuxin (17.27 ng/mL) followed by Shenyang (12.70 ng/mL), Anshan (12.63 ng/mL), Yingkou (12.23 ng/mL), Jinzhou (10.55 ng/mL), and Huludao (8.30 ng/mL), whereas the lowest was found in Dalian (5.97 ng/mL).

The compositions of PFCs in blood were compared among cities (Figure 2). The greatest contribution was from PFOS in each city ranging from 45 to 68%. However, the relative proportion of PFOA and PFHxS was different among cities. In Fuxin and Jinzhou, PFOA had the second greatest contribution which was significantly higher than that from PFHxS by about two times. By contrast, in Shenyang, Anshan, and Yingkou, the second greatest contribution was from PFHxS which was about three times higher than that from PFOA. The contributions from PFOA and PFHxS were comparable in Dalian and Huludao. In addition, the contributions of PFUdA in these two cities were significantly higher than that from other cities. The seven cities could be grouped according to the similar composition pattern of PFCs in reference to Figure 2. Fuxin and Jinzhou were grouped with high PFOA proportion, whereas Shenyang, Anshan, and

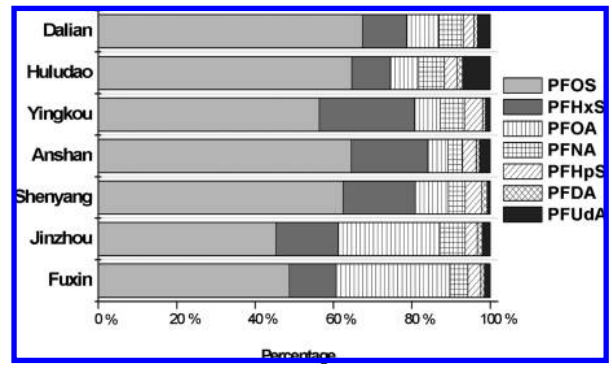

FIGURE 2. Composition profile of seven PFCs in human blood from seven cities of Liaoning province.

Yingkou were grouped with high PFHxS proportion. Although Dalian and Huludao are far from each other (>200 km), the similar profiles of PFCs in human blood grouped these two cities.

The comparison of PFCs profiles showed that there were apparent differences of human PFCs exposure between three city groups which implied varying and inconsistent human exposure source or pathway of these compounds in Liaoning province.

Comparison of PFCs in Human Blood of Shenyang. To our knowledge, among the seven cities, only the blood samples from Shenyang were analyzed for PFCs previously. The concentrations and profiles of PFCs in whole blood from Shenyang in present study were compared with the results from a previous study in which the human blood samples were collected in 2004. The arithmetical mean concentration of PFOA (1.07 ng/mL), PFNA (0.68 ng/mL), PFDA (0.23 ng/mL), and PFHxS (3.32 ng/mL) in the present study were about 2× greater than those (0.53 ng/mL for PFOA, 0.37 ng/mL for PFNA, 0.11 ng/mL for PFDA, and 2.01 ng/mL for PFHxS) reported in the previous study, which implied an possible increasing trend for these contaminants in Shenyang between 2004 and 2008. However, the mean PFOS concentration (9.57 ng/mL) in the present study was 8 times lower than that (76.64 ng/mL) in the previous study. The reason for such large differences on PFOS is unknown.

A Pilot Analysis of Human Exposure Source and Pathway of PFCs in Liaoning. The highest blood total-PFCs and PFOA level were found in Fuxin. There is one of the largest fluoropolymer manufacture centers of China in Fuxin. PFOA is an important material in the manufacture of various fluoropolymers. Therefore, the high level and proportion of PFOA in human blood collected in Fuxin could be related to residential water, local food, and air contaminated by industrial release in Fuxin. One previous study showed the high PFOA exposure in residents near a fluoropolymer production facility by residential water and home-grown fruit and vegetables in the U.S. (*25*). According to the initial findings of a study of 69 000 people who live near a PFCs manufacturing plant in Washington, West Virginia, the health effects observed in the study population were believed to have been caused by exposure to PFOA released from the plant to local water system (*33*). It was reported that the general wastewater treatment could not effectively remove PFOA (*34, 35*). A recent document reported the process wastewater of perfluorochemical manufacturer used to be discharge to the municipal waste treatment plant, which was a likely source of PFOS and PFOA in agricultural soils near Decatur, IL (*36*).

Jinzhou is located about 100 km southwest of Fuxin and no perfluoropolymer manufacture is known in Jinzhou. The comparable profiles of PFCs, especially the high proportion of PFOA in human blood from Jinzhou and Fuxin, implied that the human PFCs exposure in Jinzhou may be influenced by industrial discharge or industrial waste distribution from Fuxin through some environmental mediums, such as water, soil, and air. In Germany, a high concentration of PFOA in water of the Ruhr River was detected after PFCs contamination in an upper tributary of Ruhr River, Mohne River that was impacted by PFC-containing soil conditioner which had been mingled with industrial waste. A 4−8-fold increase in blood PFOA concentration was found in the residents near that river system (*24, 35*).

To our knowledge, there is no large fluorochemical product manufacturer in Shenyang, Anshan and Yingkou. As an important industrial region in China, the manufacture processes, such as production of electronic products, plastic products and textiles, are expected to be potential sources of PFCs. Dalian and Huludao are far from each other (>200km). In addition, the area, population, industrialization structure, and level are distinctly different between these two cities. The reason for the similar concentrations and profiles of PFCs in human blood from Dalian and Huludao was unknown. It is worth noting that although Jinzhou is close to Huludao (70 km), the distinctly different PFCs level and profile were found between blood samples from these two cities, which suggested different human exposure sources or pathways in that small region.

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Supporting Information Available

Table showing the geometric mean concentration, standard deviation (SD), minimum and maximum of seven perfluorinated alkyl compounds (ng/mL) in whole blood samples stratified by gender and age from seven cities in Liaoning, China. This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) Lehmler, H. J. Synthesis of environmentally relevant fluorinated surfactants—A review. *Chemosphere* **2005**, *58* (11), 1471–96.
(2) Hekster, F. M.; Laane, R. W.; de, V. P. Environmental and toxicity effects of perfluoroalkylated substances. *Rev. Environ. Contam. T* **2003**, *179*, 99–121.
(3) Lohmann, R.; Breivik, K.; Dachs, J.; Muir, D. Global fate of POPs: Current and future research directions. *Environ. Pollut.* **2007**, *150* (1), 150–65.
(4) Villagrasa, M.; Lopez, A. M.; Barcelo, D. Environmental analysis of fluorinated alkyl substances by liquid chromatography-(tandem) mass spectrometry: A review. *Anal. Bioanal. Chem.* **2006**, *386* (4), 953–72.
(5) Taniyasu, S.; Kannan, K.; So, M. K.; Gulkowska, A.; Sinclair, E.; Okazawa, T.; Yamashita, N. Analysis of fluorotelomer alcohols, fluorotelomer acids, and short- and long-chain perfluorinated acids in water and biota. *J. Chromatogr., A* **2005**, *1093* (1−2), 89–97.
(6) Tao, L.; Kannan, K.; Kajiwara, N.; Costa, M. M.; Fillmann, G.; Takahashi, S.; Tanabe, S. Perfluorooctanesulfonate and related fluorochemicals in albatrosses, elephant seals, penguins, and polar skuas from the Southern Ocean. *Environ. Sci. Technol.* **2006**, *40* (24), 7642–8.
(7) Smithwick, M.; Mabury, S. A.; Solomon, K. R.; Sonne, C.; Martin, J. W.; Born, E. W.; Dietz, R.; Derocher, A. E.; Letcher, R. J.; Evans, T. J.; Gabrielsen, G. W.; Nagy, J.; Stirling, I.; Taylor, M. K.; Muir, D. C. Circumpolar study of perfluoroalkyl contaminants in polar bears (*Ursus maritimus*). *Environ. Sci. Technol.* **2005**, *39* (15), 5517–23.
(8) Fei, C.; McLaughlin, J. K.; Tarone, R. E.; Olsen, J. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. *Environ. Health Perspect.* **2007**, *115* (11), 1677–82.
(9) Kennedy, G. L.; Butenhoff, J. L.; Olsen, G. W.; O, C. J.; Seacat, A. M.; Perkins, R. G.; Biegel, L. B.; Murphy, S. R.; Farrar, D. G. The toxicology of perfluorooctanoate. *Crit. Rev. Toxicol.* **2004**, *34* (4), 351–84.
(10) Kannan, K.; Corsolini, S.; Falandysz, J.; Fillmann, G.; Kumar, K. S.; Loganathan, B. G.; Mohd, M. A.; Olivero, J.; Van, W. N.; Yang, J. H.; Aldoust, K. M. Perfluorooctanesulfonate and related fluorochemicals in human blood from several countries. *Environ. Sci. Technol.* **2004**, *38* (17), 4489–95.
(11) Apelberg, B. J.; Witter, F. R.; Herbstman, J. B.; Calafat, A. M.; Halden, R. U.; Needham, L. L.; Goldman, L. R. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. *Environ. Health Perspect.* **2007**, *115* (11), 1670–6.
(12) Harada, K.; Koizumi, A.; Saito, N.; Inoue, K.; Yoshinaga, T.; Date, C.; Fujii, S.; Hachiya, N.; Hirosawa, I.; Koda, S.; Kusaka, Y.; Murata, K.; Omae, K.; Shimbo, S.; Takenaka, K.; Takeshita, T.; Todoriki, H.; Wada, Y.; Watanabe, T.; Ikeda, M. Historical and geographical aspects of the increasing perfluorooctanoate and perfluorooctane sulfonate contamination in human serum in Japan. *Chemosphere* **2007**, *66*, 293–301.

(13) Olsen, G. W.; Huang, H. Y.; Helzlsouer, K. J.; Hansen, K. J.; Butenhoff, J. L.; Mandel, J. H. Historical comparison of perfluorooctanesulfonate, perfluorooctanoate, and other fluorochemicals in human blood. *Environ. Health Perspect.* **2005**, *113* (5), 539–45.
(14) Olsen, G. W.; Mair, D. C.; Church, T. R.; Ellefson, M. E.; Reagen, W. K.; Boyd, T. M.; Herron, R. M.; Medhdizadehkashi, Z.; Nobiletti, J. B.; Rios, J. A.; Butenhoff, J. L.; Zobel, L. R. Decline in perfluorooctanesulfonate and other polyfluoroalkyl chemicals in American Red Cross adult blood donors, 2000−2006. *Environ. Sci. Technol.* **2008**, *42* (13), 4989–95.
(15) Spliethoff, H. M.; Tao, L.; Shaver, S. M.; Aldous, K. M.; Pass, K. A.; Kannan, K.; Eadon, G. A. Use of newborn screening program blood spots for exposure assessment: declining levels of perluorinated compounds in New York State infants. *Environ. Sci. Technol.* **2008**, *42* (14), 5361–7.
(16) Calafat, A. M.; Wong, L. Y.; Kuklenyik, Z.; Reidy, J. A.; Needham, L. L.; Polyfluoroalkyl chemicals in the, U. S. population: data from the National Health and Nutrition Examination Survey (NHANES) 2003−2004 and comparisons with NHANES 1999−2000. *Environ. Health Perspect.* **2007**, *115* (11), 1596–602.
(17) Jin, Y.; Saito, N.; Harada, K. H.; Inoue, K.; Koizumi, A. Historical trends in human serum levels of perfluorooctanoate and perfluorooctane sulfonate in Shenyang, China. *Tohoku J. Exp. Med.* **2007**, *212* (1), 63–70.
(18) Karrman, A.; Ericson, I.; van Bavel, B.; Darnerud, P. O.; Aune, M.; Glynn, A.; Lignell, S.; Lindstrom, G. Exposure of Perfluorinated Chemicals through Lactation: Levels of Matched Human Milk and Serum and a Temporal Trend, 1996−2004, in Sweden. *Environ. Health Perspect.* **2007**, *115*, 226–230.
(19) Wilhelm, M.; Kraft, M.; Rauchfuss, K.; Jürgen, H. Assessment and management of the first german case of a contamination with perfluorinated compounds (PFC) in the Region Sauerland, North Rhine-Westphalia. *J. Toxicol. Environ. Health A* **2008**, *71* (11), 725–733.
(20) Shoeib, M.; Harner, T.; Ikonomou, M.; Kannan, K. Indoor and outdoor air concentrations and phase partitioning of perfluoroalkyl sulfonamides and polybrominated diphenyl ethers. *Environ. Sci. Technol.* **2004**, *38* (5), 1313–20.
(21) Kubwabo, C.; Stewart, B.; Zhu, J.; Marro, L. Occurrence of perfluorosulfonates and other perfluorochemicals in dust from selected homes in the city of Ottawa, Canada. *J. Environ. Monit.* **2005**, *7* (11), 1074–8.
(22) Tittlemier, S. A.; Pepper, K.; Seymour, C.; Moisey, J.; Bronson, R.; Cao, X. L.; Dabeka, R. W. Dietary exposure of Canadians to perfluorinated carboxylates and perfluorooctane sulfonate via consumption of meat, fish, fast foods, and food items prepared in their packaging. *J. Agric. Food Chem.* **2007**, *55* (8), 3203–10.
(23) Ericson, I.; Nadal, M.; van, B. B.; Lindstrom, G.; Domingo, J. L. Levels of perfluorochemicals in water samples from Catalonia, Spain: is drinking water a significant contribution to human exposure. *Environ. Sci. Pollut. Res. Int.* **2008**, *15* (7), 614–9.
(24) Holzer, J.; Midasch, O.; Rauchfuss, K.; Kraft, M.; Reupert, R.; Angerer, J.; Kleeschulte, P.; Marschall, N.; Wilhelm, M. Biomonitoring of perfluorinated compounds in children and adults exposed to perfluorooctanoate-contaminated drinking water. *Environ. Health Perspect.* **2008**, *116* (5), 651–7.
(25) Emmett, E. A.; Shofer, F. S.; Zhang, H.; Freeman, D.; Desai, C.; Shaw, L. M. Community exposure to perfluorooctanoate: relationships between serum concentrations and exposure sources. *J. Occup. Environ. Med.* **2006**, *48* (8), 759–70.
(26) Houde, M.; Martin, J. W.; Letcher, R. J.; Solomon, K. R.; Muir, D. C. Biological monitoring of polyfluoroalkyl substances: A review. *Environ. Sci. Technol.* **2006**, *40* (11), 3463–73.
(27) Deon, J. C.; Mabury, S. A. Production of perfluorinated carboxylic acids (PFCAs) from the biotransformation of polyfluoroalkyl phosphate surfactants (PAPS): exploring routes of human contamination. *Environ. Sci. Technol.* **2007**, *41* (13), 4799–805.
(28) Yeung, L. W.; So, M. K.; Jiang, G.; Taniyasu, S.; Yamashita, N.; Song, M.; Wu, Y.; Li, J.; Giesy, J. P.; Guruge, K. S.; Lam, P. K. Perfluorooctanesulfonate and related fluorochemicals in human blood samples from China. *Environ. Sci. Technol.* **2006**, *40* (3), 715–20.
(29) Hansen, K. J.; Clemen, L. A.; Ellefson, M. E.; Johnson, H. O. Compound-specific, quantitative characterization of organic fluorochemicals in biological matrices. *Environ. Sci. Technol.* **2001**, *35* (4), 766–70.
(30) Hornung, R. W.; Reed, L. D. Estimation of average concentration in the presence of nondetectable values. *Appl. Occup. Environ. Hyg.* **1990**, *5*, 46–51.
(31) Ericson, I.; Gomez, M.; Nadal, M.; van, B. B.; Lindstrom, G.; Domingo, J. L. Perfluorinated chemicals in blood of residents in Catalonia (Spain) in relation to age and gender: a pilot study. *Environ. Int.* **2007**, *33* (5), 616–23.
(32) Karrman, A.; Mueller, J. F.; van, B. B.; Harden, F.; Toms, L. M.; Lindstrom, G. Levels of 12 perfluorinated chemicals in pooled australian serum, collected 2002−2003, in relation to age, gender, and region. *Environ. Sci. Technol.* **2006**, *40* (12), 3742–8.
(33) Environment News Service Chemical used to make non-stick coatings may be harmful to health—research. http://www.hsc.wvu.edu/som/cmed/news/archive/may2008environmentalexpert_c8.pdf (accessed May 14, 2008).
(34) Loos, R.; Wollgast, J.; Huber, T.; Hanke, G. Polar herbicides, pharmaceutical products, perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA), and nonylphenol and its carboxylates and ethoxylates in surface and tap waters around Lake Maggiore in Northern Italy. *Anal. Bioanal. Chem.* **2007**, *387* (4), 1469–78.
(35) Skutlarek, D.; Exner, M.; Farber, H. Perfluorinated surfactants in surface and drinking waters. *Environ. Sci. Pollut. Res. Int.* **2006**, *13* (5), 299–307.
(36) Renner, R. EPA finds record PFOS, PFOA levels in Alabama grazing fields. *Environ. Sci. Technol.* **2008**, *43* (5), 1245–46.

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