Perfluorinated Compounds in Whole Blood Samples from Infants, Children, and Adults in China

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Two hundred and forty five human blood (whole blood) samples from Chinese donors aged from 0 to 90 yrs were analyzed for 10 perfluorinated compounds (PFCs). Perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) were the most abundant PFCs found in blood. The median concentration of PFOS was lower in nonadults (i.e., infants, toddlers, children, and adolescents) (2.52−5.55 ng/mL) than in adults (8.07 ng/mL). However, median concentration of PFOA in nonadults (1.23−2.42 ng/mL) was higher than that found in adults (1.01 ng/mL). A significant increase in PFOS ($r = 0.468$, $p < 0.01$) and perfluorohexane sulfonate (PFHxS) ($r = 0.357$, $p < 0.01$) concentrations with age was found, while PFOA concentrations ($r = -0.344$, $p < 0.01$) were negatively correlated with age. No significant gender-related differences in PFC concentrations were found across all ages. The composition profiles of PFCs, as identified by principal component analysis, varied for each age group; this suggested differences in sources and pathways of exposure to PFCs for different age groups. Based on the blood PFC concentration, we estimated the daily intake of PFOS by adults using a one-compartment toxicokinetic model. The modeled daily intake of PFOS agreed well with the calculated daily intake via diet and indoor dust (0.74 vs 1.19 ng/kg b.w. for males, 1.20 vs 1.15 ng/kg b.w. for females) suggesting that dietary intake and dust ingestion are the major exposure routes to PFOS exposure in China. This is the first comprehensive study on PFCs in human blood from infants, toddlers, children, and adolescents in China. The data are valuable for understanding the sources and pathways of human exposure to PFCs for different age groups.

Introduction

Perfluorinated compounds (PFCs) comprise of a large group of man-made chemicals consisting of a fully fluorinated alkyl chain, with different polar functional groups (*1*). Since the 1950s, PFCs have been used worldwide in a variety of industrial and commercial products such as lubricants, paints, polishes, fire-fighting foams, and food packaging (*2, 3*). In recent years, concerns about the occurrence of PFCs in foods (*4–6*), indoor dust (*5, 7, 8*), and humans (*9–18*) have been raised.

Perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are the most abundant PFCs in humans around the world (*2, 9–12*). In Australia (*9*), a study on PFCs in pooled serum samples suggested that the concentrations of PFOS were higher in adult males than in adult females, while no gender differences were found for serum pools from children (<12 yrs old). Similarly, higher concentrations of PFCs in adult males than in adult females have been reported in studies from China (*10*), the U.S. (*11*), and Japan (*12*). However, gender-related differences in PFC concentrations were not obvious in several investigations (*13, 14*). No gender-related difference was found in the concentrations of PFOS and PFOA in human serum samples collected from the U.S. (*13*) and Norway (*14*). Furthermore, the age-related accumulation of PFCs in humans is still not clear (*11, 14–17*). An increase in PFOS concentration with age was reported in Australia (*15*), Germany (*16*), and Norway (*14*). However, no age-related increase in the concentrations of PFOS was found in the U.S. (*11, 17*), and in some Asian countries (*17*). Lack of consistency in the results of age-related increase in PFC levels reported in previous studies was probably due to the existence of several confounding demographic variables (diet, occupation, age, etc.) including the study design (number of samples and age groups examined) which can influence the concentrations of PFCs.

In the U.S., a declining trend in PFOS concentration in human blood was found after 2002 (*14, 18*), coinciding with the phase-out in PFOS production in that country (*19*). However, an increasing trend in serum levels of PFOS and PFOA was found from 1987 to 2002 in Shenyang, China (*20*). Previous studies on PFCs in the Chinese general population focused only on adults, and showed that PFOS levels in Chinese adults were higher than in most other countries (*10*). In this study, we report age- and gender-related differences in the concentration of PFCs in 245 human blood samples collected from donors aged from 0 to 90 yrs. Availability of donors from a wide age range provided an opportunity to characterize and stratify these subjects into different age groups. This is the first study to report PFC concentrations in human blood from infants, toddlers, children, and adolescents (0−18 yrs) in China. Furthermore, we analyzed the profiles of PFCs, for each age group to enable a better understanding of potential sources and pathways of exposures.

Materials and Methods

Blood samples were extracted by ion-pair method as reported in other studies (*17, 18*); concentrations of analyzed PFCs were determined by using an Agilent 1100 series high performance liquid chromatograph (HPLC) coupled with an Applied Biosystems API 2000 electrospray triple-quadrupole mass spectrometer (ESI-MS/MS). Details regarding reagents and chemicals, sample preparation and extraction procedures, blank/recovery experiments, instrumental methods

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TABLE 1. PFC Concentrations (ng/mL) in Blood from Infants, Toddlers, Children, Adolescents, and Adults in China

		PFBS	PFHxS	PFOS	PFDS	PFOSA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
total (n = 245)	detection[a] (%)	0	83	100	0	13	97	89	86	81	2
	median (mean)	<0.19	0.23 (0.36)	4.41 (7.19)	<0.59	<0.10 (0.08)	2.05 (2.45)	0.65 (0.92)	0.38 (0.59)	0.76 (0.90)	<0.21 (0.12)
	range	<0.19	<0.22−2.64	0.73−105	<0.59	<0.10−1.28	<0.56−15.2	<0.10−16.4	<0.20−20.0	<0.10−3.65	<0.21−1.55
age group[b]											
infants (n = 14)	median (mean)	<0.19	0.11 (0.25)	2.68 (4.20)	<0.59	<0.10	1.70 (2.67)	0.38 (0.52)	0.25 (1.72)	0.18 (0.62)	<0.21
	range	<0.19	<0.22−0.77	0.76−16.1	<0.59	<0.10	0.35−11.0	<0.10−2.03	<0.20−20.0	<0.10−2.50	<0.21
toddlers (n = 85)	median (mean)	<0.19	0.14 (0.24)	2.52 (3.79)	<0.59	<0.10	2.42 (2.97)	0.55 (1.20)	0.33 (0.50)	0.69 (0.92)	<0.21 (0.12)
	range	<0.19	<0.22−1.09	0.94−23.3	<0.59	<0.10−0.17	0.36−15.2	<0.10−16.4	<0.20−3.11	<0.10−3.65	<0.21−1.55
children (n = 85)	median (mean)	<0.19	0.27 (0.38)	5.55 (7.05)	<0.59	<0.10	2.19 (2.49)	0.74 (0.82)	0.43 (0.54)	0.78 (0.94)	<0.21 (0.13)
	range	<0.19	<0.22−2.41	1.52−32.9	<0.59	<0.10−0.18	0.30−6.37	<0.10−2.22	<0.20−1.83	<0.10−2.97	<0.21−0.29
adolescents (n = 19)	median (mean)	<0.19	0.18 (0.31)	4.36 (6.79)	<0.59	<0.10	1.23 (1.53)	0.71 (0.63)	0.52 (0.49)	0.89 (0.82)	<0.21
	range	<0.19	<0.22−1.09	0.82−25.6	<0.59	<0.10−0.11	<0.56−3.22	<0.10−1.29	<0.20−1.20	<0.10−2.02	<0.21
adults (n = 42)	median (mean)	<0.19	0.40 (0.62)	8.07 (15.5)	<0.59	<0.10 (0.12)	1.01 (1.58)	0.71 (0.81)	0.40 (0.58)	0.64 (0.92)	<0.21
	range	<0.19	<0.22−2.64	0.73−105	<0.59	<0.10−1.28	<0.56−12.9	<0.10−2.75	<0.20−3.06	<0.10−3.19	<0.21
sexes											
male (n = 163)	median (mean)	<0.19	0.24 (0.37)	4.42 (7.02)	<0.59	<0.11 (0.09)	1.97 (2.23)	0.63 (0.83)	0.39 (0.63)	0.75 (0.91)	<0.21
	range	<0.19	<0.22−2.64	0.73−76.5	<0.59	<0.10−1.28	<0.56−11.0	<0.10−9.57	<0.20−20.0	<0.10−3.65	<0.21−1.55
female (n = 82)	median (mean)	<0.19	0.22 (0.34)	4.46 (7.79)	<0.59	<0.11 (0.07)	2.04 (2.74)	0.65 (1.07)	0.33 (0.50)	0.76 (0.96)	<0.21
	range	<0.19	<0.22−2.53	0.73−105	<0.59	<0.10−0.19	<0.56−15.2	<0.10−16.4	<0.20−3.06	<0.10−3.19	<0.21

[a] Detection = frequency of detection. [b] Age group including infants (0−1 yrs), toddlers (1−5 yrs), children (5−10 yrs), adolescents (10−18 yrs), and adults (18−90 yrs).

used in the present study are given in the Supporting Information (SI).

Sample Collection. As shown in SI Figure S1, Nanchang city (28°38N, 115°56E), the capital of Jiangxi province located in southern China, was selected for sampling. The estimated population of the city is 4.0 million. During February−March 2009, 245 human blood samples were obtained from participants aged 0−90 yrs. The blood samples were collected (1 mL) as part of a routine clinical testing or for heavy metal (e.g., lead) analysis. The residual sample left after the clinical testing was used for PFCs analysis in our study. Participants' age, gender, and the date of blood collection were available for each sample. The detailed demographic information including sample size, age and gender are shown in SI Table S1. All the samples were stratified according to age and gender as infants (0−1 yrs), toddlers (1−5 yrs), children (5−10 yrs), adolescents (10−18 yrs), and adults (18−90 yrs), and were stored in polypropylene containers at −20 °C until analysis. The blood collection was approved by Institutional Review Board of Nankai University, China.

Quality Assurance and Quality Control. Our laboratory participates in several intercomparison studies and proficiency testing including analysis serum samples provided by the Arctic Monitoring and Assessment Program, every 6 months. Our results for PFCs in serum samples were always within ±10% of the actual values. In this study, $^{13}C_4$-PFOS, $^{13}C_4$-PFOA, $^{13}C_2$-PFNA, and $^{13}C_2$-PFDA were spiked as internal standards into blood samples prior to the addition of reagents for extraction. Recoveries of $^{13}C_4$-PFOS, $^{13}C_4$-PFOA, $^{13}C_2$-PFNA, and $^{13}C_2$-PFDA (n = 245) spiked into each of the sample were 87 ± 5%, 168 ± 10%, 164 ± 15%, and 180 ± 27%, respectively. High recoveries for PFOA, perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA) were due to ionization enhancement occurred in the electrospray interface. In order to further evaluate the matrix effect, each of the internal standard response was compared (5 ng/mL) (n = 5, internal standards were spiked after sample extraction) with the standards in pure methanol; prominent ionization enhancement was found for $^{13}C_4$-PFOA (+51%), $^{13}C_2$-PFNA (+34%), and $^{13}C_2$-PFDA (+ 83%). Therefore, the reported concentrations of PFOA, PFNA, and PFDA in each sample were corrected by the recoveries of respective internal standards. The concentrations of other six PFCs, perfluorobutane sulfonate (PFBS), perfluorohexane sulfonate (PFHxS), perfluorodecane sulfonate (PFDS), perfluorooctane sulfonamide (PFOSA), perfluoroundecanoic acid (PFUnDA), and perfluorododecanoic acid (PFDoDA), were not adjusted for recoveries, and concentrations of these compounds in blood samples may be biased toward lower end of the values for PFHxS, and higher end of the values for PFUnDA. PFBS, PFDS, PFOSA, and PFDoDA were found only in a few of samples (0−13%) (Table 1). Method precision was excellent, with relative standard deviations of six analyses of the same blood samples was less than 10% for PFHxS, PFOS, and PFDS, and 10−20% for PFBS, PFOSA, PFNA, PFDA, PFUnDA, and PFDoDA.

Solvents, blood collection tubes, and method blanks (performance of blanks were listed in Supporting Information) were checked for the presence of target PFCs analyzed in this study. Blanks contained PFOA at trace concentrations. Reported PFOA concentrations were subtracted from blank values. The limit of quantitation (LOQ) was determinated as the lowest concentration of PFC in calibration curve with a signal-to-noise ratio of 10, with sample volume and dilution factors included in the calculation. The LOQ for PFOS and PFOA was 0.17 and 0.56 ng/mL, respectively, and for other PFCs it ranged from 0.10 to 0.59 ng/mL.

Modeling of Exposures Based on Blood PFC Levels. In previous studies (*21–23*), pharmacokinetic models have been used for the estimation of daily intake of contaminants by using biomonitoring data. Ritter et al. (*21*) developed a multi-individual pharmacokinetic model and estimated the daily intake of POPs. However, this model may not be applicable for Chinese population. A simple one-compartment toxicokinetic model is considered only valid for steady state conditions (*22, 23*) of blood PFC level. No age-related accumulation of PFOS (r = 0.050, p = 0.751), and PFOA (r = 0.287, p = 0.690) level in blood was observed for adults in China, and we assumed a steady state condition exists in adults. The daily intake of PFCs by adults was estimated based on the blood PFC concentrations using the following equation described by Fromme et al. (*22*) and Thompson et al. (*23*). The change in blood concentration (C_p) resulting from a given exposure dose (E) can be described by the following equation:

$$\frac{\Delta C_p}{\Delta t} = E - k \times V_d \times C_p$$

where V_d is the apparent volume of distribution (mL/kg), and k is the first-order rate constant for PFC elimination per day $= 0.693/t_{1/2}$, at steady-state conditions, where $\Delta C_p/\Delta t = 0$,

$$E = k \times V_d \times C_p$$

and

$$E = 0.693/t_{1/2} \times V_d \times C_p$$

For females, the total clearance was corrected by menstrual serum loss. As described by Harada et al. (*24*) menstrual serum loss was assumed to be 42 mL/month = 0.025 mL/kg/day, assuming an average body weight of 55 kg (*25*). For PFOS and PFOA, median half-lives were 1661 days (4.55 yrs) and 1257 days (3.44 yrs) (*26*), respectively. In accordance with Thompson et al. (*23*), we used a volume distribution of 230 mL/kg for PFOS and 170 mL/kg for PFOA.

Statistical Analysis. The Spearman's rank correlation was used to assess the relationship between age and PFC levels, and among various PFCs in the sample; the differences in PFC concentrations between male and female were evaluated using one way analysis of variance (ANOVA). The average proportion of individual PFCs to total PFC concentrations in human blood from each age group (e.g., 0−1, 1−2, 2−3, 3−4, 4−5, 5−6, 6−7, 7−8, 8−10, 10−18, 18−60, 60−70, 70−80, 80−90 yrs group) was examined by principal components analysis (PCA) to delineate potential pattern in the data. The concentrations of PFCs were log-transformed for PCA using STATGRAPHICS Centurion XV (StatPoint, Inc., Herndon, VA). Concentrations below the LOQ were assigned half the value of the LOQ for statistical analysis. One-way ANOVA and Spearman's correlation (r) were analyzed with SPSS 17.0 (Chicago, IL).

Results and Discussion

PFCs in Human Blood. Concentrations of 10 PFCs analyzed in human blood samples from infants (0−1 yrs), toddlers (1−5 yrs), children (5−10 yrs), adolescents (10−18 yrs), and adults (18−90 yrs) are given in Table 1. PFOS (100%), PFOA (97%), PFNA (89%), PFDA (86%), PFHxS (83%), and PFUnDA (81%) were detected frequently, while PFBS, PFDS, PFOSA, and PFDoDA were found less frequently (<15%). Therefore, results for PFBS, PFDS, PFOSA, and PFDoDA are not discussed further. PFOS was found at the highest median concentration, 4.41 ng/mL (range: 0.76 to 105 ng/mL), followed by PFOA at 2.05 ng/mL (<0.56 to 15.2 ng/mL), PFUnDA at 0.76 ng/mL, PFNA at 0.65 ng/mL, PFDA at 0.38 ng/mL, and PFHxS at 0.23 ng/mL.

In infants, toddlers, children, and adolescents (nonadults; ages <18 yrs), the median concentrations of PFOS and PFHxS ranged from 2.52 to 5.55 ng/mL and from 0.11 to 0.27 ng/mL (Table 1), respectively, which were 1.5−2.5 times lower than the concentrations in adults (8.07 ng/mL for PFOS, and 0.40 ng/mL for PFHxS); however, the median concentration of PFOA (1.23−2.42 ng/mL) was higher in nonadults, than in adults (1.01 ng/mL). Furthermore, infants' blood contained the greatest mean concentration of PFDA compared to other age groups; this is due to an anomalously high concentration of PFDA found in an infant at 20.0 ng/mL (Table 1). This outlier PFDA concentration value was excluded from further discussions.

The geometric mean concentrations (GM) of PFOS, PFDA, and PFUnDA in adults from this study (from Jiangxi Province located in southern China) were greater than the concentrations reported earlier from Liaoning Province located in northern China (*27*) (SI Table S2). In contrast, the GM concentration of PFHxS was lower in Jiangxi Province than in Liaoning Province (SI Table S2). Furthermore, the composition profile of PFCs in blood samples from adults was quite different between these two provinces (SI Figure S2). PFOA accounted for 8.4% of the total PFC concentrations in Jiangxi whereas in Fuxin and Jinzhou city of Liaoning Province, PFOA accounted for 30% of the total PFC concentrations in blood (*27*). This is attributable to the existence of a largest fluoropolymer manufacturer in Fuxin, and industrial discharge or industrial waste from Fuxin can influence human PFCs exposure in Jinzhou, which is located within 100 km southwest of Fuxin. The differences in concentrations and profiles of PFCs in human blood between Jiangxi and Liaoning Province suggest different exposure routes in the general population between these two provinces in China. The concentrations of PFOS and PFOA in blood from Chinese adults were similar to concentrations reported for the general populations from Australia (*9*), Norway (*14*) and Canada (*28*), but less than those reported for Germany (*29*).

TABLE 2. Probabaility of Significance Associations (Spearmans Rank Correlation;*p*-Value)between Individual Age and Corresponding Concentrations of PFCs[a]

	(0−90 yrs)			nonadults (0−18 yrs)		
	M and F[b]	male	female	M and F	male	female
PFHxS	0.357**	0.343**	0.326**	0.208*	0.196*	0.144
PFOS	0.468**	0.417**	0.547**	0.383*	0.326**	0.496**
PFOA	−0.344**	−0.425**	−0.139	−0.127	−0.199*	0.093
PFNA	0.061	−0.041	0.302**	0.085	−0.022	0.362**
PFDA	0.110	−0.021	0.320**	0.172*	0.051	0.343**
PFUnDA	0.017	−0.052	0.188	0.070	−0.012	0.279*

[a] Level of significance donated as $p < 0.05$(*), $p < 0.01$(**). [b] M and F = male and female.

Age-Dependent Accumulation of PFCs. To our knowledge, comprehensive study on age related differences in PFC accumulation in human blood (or serum) is limited (*9, 14*). This is the first study to report PFC levels in individual whole blood samples ($n = 245$) collected from donors with an age range of 0−90 yrs. Large sample size and wide age range enabled better understanding of age-related accumulation of PFCs in humans. In this study, the correlations between individual age and corresponding concentration of each PFC were evaluated by Spearman's rank correlation.

PFC concentrations varied by age in China (Table 2, Figure 1, SI Figure S3). For all donors (0−90 yrs), a significant increase in PFOS ($r = 0.468$, $p < 0.01$) and PFHxS ($r = 0.357$, $p < 0.01$) concentrations with age was found; while concentrations of PFOA ($r = -0.344$, $p < 0.01$) exhibited a significant negative correlation with age (Table 2, Figure 1); no significant association between age and concentrations of PFNA, PFDA and PFUnDA was found in the present study (SI Figure S3). For nonadults (0−18 yrs), similar results were obtained between PFC concentrations and age (Table 2), while a lack of relationship between PFOA concentration and age was found. Furthermore, it is important to note that concentrations of long chain perfluorocarboxylic acids (PFCAs), such as PFNA, PFDA, and PFUnDA in nonadult females exhibited a positive correlation with age (Table 2), suggesting that the accumulation pattern of long chain PFCAs may be gender-specific. The reason for such age-related accumulation pattern of long chain PFCAs in nonadult females is unknown.

In a previous study from Liaoning Province in China (*27*), blood concentrations of PFCs were significantly higher in elderly people than in young people. However, another Chinese study found a lack of association between age and concentrations of PFOA, PFOS, and PFHxS in blood (*10*). A

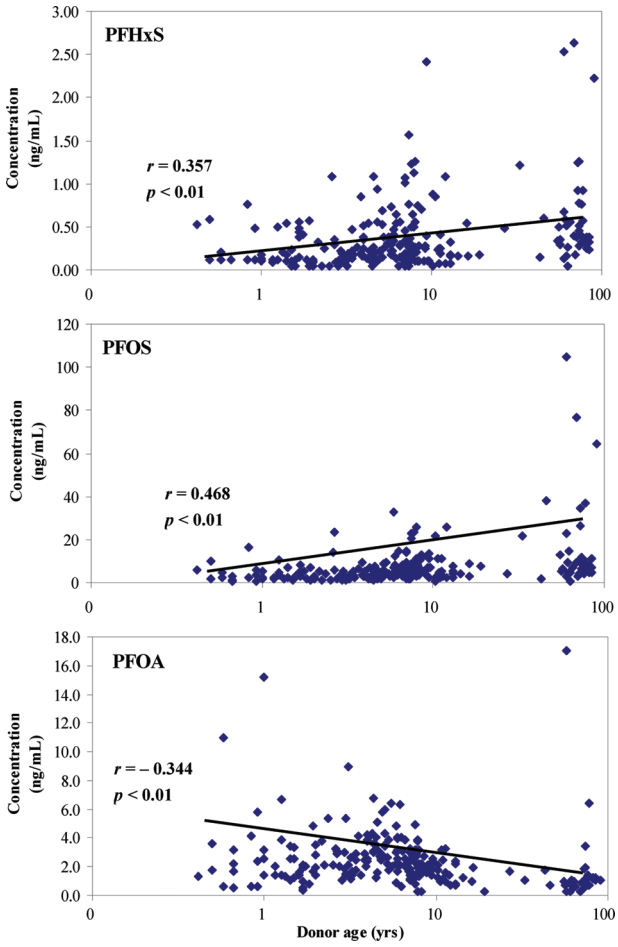

FIGURE 1. Relationship of PFHxS, PFOS, and PFOA concentrations in human blood with age of donors from China (values below the LOQ were treated as zero). Relationships of PFNA, PFDA, PFUnDA concentrations with age are shown in SI Figure S3.

significant increase in concentrations of PFCs, especially PFNA, PFDA, PFUnDA, and perfluorotetradecanoic acid (PFTrDA), with age was found in Norway (*14*), Canada (*30*), and Germany (*16*). In contrast, higher PFC concentrations (excluding PFOS) were found in children than in adults in Australia (*9*). Lack of consistent age-related increase in body burdens of PFCs may be attributed to demographic factors that influence the concentrations, for example, elimination, lifestyle, history of exposure, and some physiological factors (*15*).

A possible reason for significant positive correlation between blood PFOS, and PFHxS concentration with age may be related to dietary intake, especially fish and seafood that contain high levels of PFOS in China (*4*). In an earlier study (*5*), we calculated the daily intake of PFCs in China, and found that fish and seafood are the major exposure source to PFOS (79%) and PFHxS (88%) exposure by adults. Furthermore, a positive correlation between PFOS and PFHxS concentrations in human blood was found in our study (SI Table S3), suggesting that the sources of human exposure to PFOS and PFHxS are common or related; this finding results in that similar age-related patterns in humans were found for PFOS and PFHxS.

Very few studies have reported a decrease in PFOA levels in blood with age (*9, 31*). The reason for the negative association of PFOA concentration with age may be due to high exposures in infants and toddlers; breast milk and dust ingestion are major sources of PFOA exposures in infants and toddlers. In our early study (*5*), we found that the contribution of dust ingestion to daily intake of PFOA was 3× higher in infants and toddlers than in adults (*5*). In China, concentration of PFOA (median: 0.05 ng/mL) was low in human serum samples collected in 1990 (*20*), therefore, we hypothesize that donors ≥19 yrs of age in the present study (born in 1990 or before) were exposed to small amounts of PFOA via breast milk or dust in their early life stages (*20*), compared to current donors of ages 0−8 yrs (>4 ng/mL PFOA was found in human serum collected in 2002, in China (*20*)), and this is another possible reason for the negative association of PFOA concentration with age.

Gender-Related Accumulation of PFCs. In general, no gender difference in concentrations of PFCs was found ($p > 0.05$, one-way ANOVA) across all ages, although median concentrations of PFOS, PFOA, PFNA, and PFUnDA were slightly higher in females than in males (Table 1). Similarly, an earlier study showed no significant difference in PFC concentrations between both sexes in Liaoning Province, China (*27*). However, another study from China showed significantly higher PFOS and PFHxS concentrations in males than in females (*10*). In other countries, significantly higher PFC concentrations in males than in females were found in the U.S. (*11*), Japan (*12*), and Canada (*30*), but no significant gender-related differences were found in samples from Norway (*14*). The lack of consistency in gender related differences in PFC levels in humans between the present study and other studies, might due to differences in the study design of the studies, such as sample size, and sampling location, etc.

We evaluated the gender-related accumulation for donors of age groups, 0−18, 18−60, and 60−90 yrs. No gender-related accumulation of PFCs were found for these three age categories, except for females with 60−90 yrs had higher concentration of PFNA ($p < 0.05$) and PFDA ($p < 0.05$) than males. This finding is inconsistent with the results reported in previous studies, which showed more pronounced gender differences in younger people than in older people (*11*), and adult males had greater mean PFOS and PFOA concentrations than 20−50 yrs old females (*24*). The effect of menstruation on gender-related differences in PFC concentration was not observed for 18−60 yrs donors. However, the statistically power is low for this age group (six males and three females).

Human Exposure Characterization Based on Age-Dependent PFC Profiles. PCA of PFC profiles in blood samples showed that PC1 and PC2 accounting for 48% and 30% of the total variances (Figure 2), respectively. The plot of loadings for PC1 against PC2 showed two-dimensional distribution in PFC profiles for age groups into four clusters (represented as A, B, C, and D in Figure 2). The first component, PC1 (48%), was significantly correlated with PFDA ($r = 0.84$; correlation coefficient), PFUnDA ($r = 0.66$), PFOS ($r = 0.57$), PFNA ($r = 0.64$), and PFHxS ($r = 0.56$). The second component, PC2 (30%), was correlated with PFOA ($r = 0.73$), PFHxS ($r = -0.73$), PFOS ($r = -0.77$), and PFNA ($r = 0.41$) (SI Figure S4).

Clusters A, B, C, and D comprised of infants and toddlers (0−5 yrs), children (5−10 yrs), adolescents (10−18 yrs), and adults (18−90 yrs), respectively (Figure 3). In general, the proportion of PFOS in total PFC concentrations ranged from 42% in cluster A (infants and toddlers) to 77% in cluster D (adults), which generally showed an increasing trend with age. In contrast, the relative composition of PFOA in total PFC concentrations in blood showed a declining trend with age, and ranged from 7% in cluster D (adults) to 29% in cluster A (infants and toddlers). These four clusters were characterized by varying proportions of individual PFCs within the total PFC concentrations (Figure 3). A similar profile pattern of relative median concentration of each PFC was found for each age group (SI Figure S5). Samples in cluster A contained an elevated proportion of PFOA. This

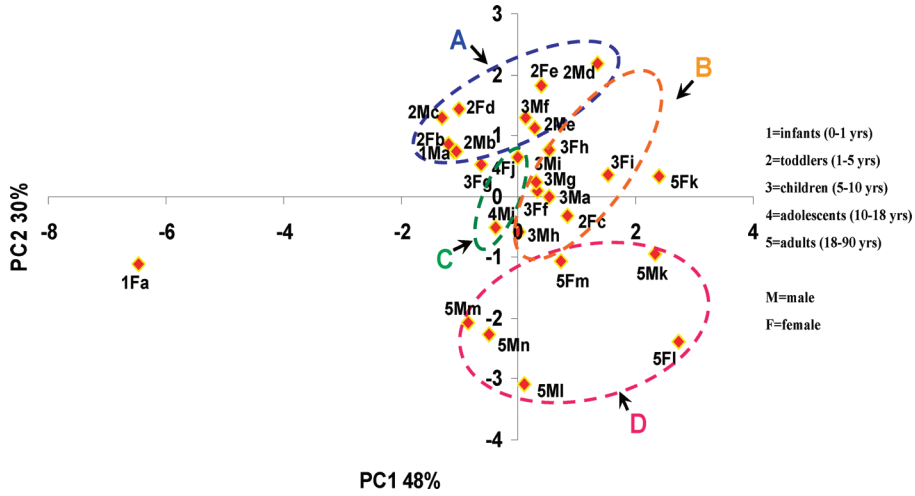

FIGURE 2. Plot of first two factors of principal component analysis of levels of six PFCs in whole blood from China. The encircled clusters identified as A, B, C, and D represent samples for infants and toddlers, children, adolescents and adults, respectively; small letters such as a, b, c, d, e, f, g, h, i, j, k, l, m, n represent 0−1, 1−2, 2−3, 3−4, 4−5, 5−6, 6−7, 7−8, 8−10, 10−18, 18−60, 60−70, 70−80, 80−90 yrs age-groups, respectively.

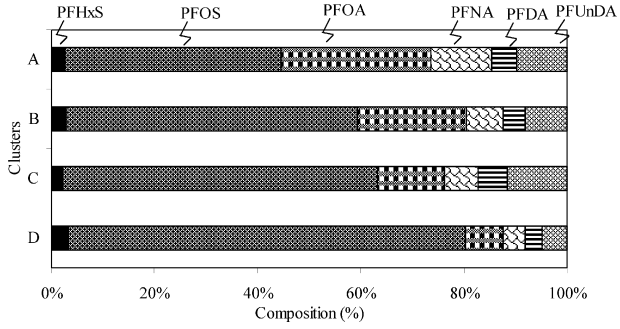

FIGURE 3. PFCs composition (%) in four clusters A, B, C, and D as identified by principal component analysis shown in Figure 2.

profile, as mentioned earlier, is expected to be related to specific exposure sources such as dust ingestion. Elevated concentrations of PFOA have been found in indoor dust in China (mean concentration: 204 ng/g for PFOA, 4.9 ng/g for PFOS (*5*)). Cluster D contained elevated proportion of PFOS; this profile suggests PFOS exposures in adults. Fish and seafood have been found to be the major contributors of PFOS exposure for adults (*5*). In general, PCA suggests the existence of a variety of exposure patterns of PFCs among several age groups.

The relationship among concentrations of various PFCs for each age group was examined by Spearman's rank correlation (SI Table S3). A significant correlation between concentrations of PFOS and PFHxS, PFOS and PFNA, PFHxS, and PFOA, were found for all age groups (SI Table S3). The correlation between PFOS and PFHxS suggests that the sources of human exposure to PFOS and PFHxS are related, as PFHxS occurs as an impurity in PFOS-based products (*32*). The correlation between PFOS and PFNA, and PFHxS and PFOA, are interesting and needs further investigation. Furthermore, there were statistically significant positive correlations between PFNA and PFOA, PFNA and PFDA, PFNA and PFUnDA, and PFDA and PFUnDA for all age groups. PFOA, PFNA, PFDA, and PFUnDA can be formed from degradation of fluorotelomer alcohols (FTOHs) (*33*). A significant positive relationship among PFOA, PFNA, PFDA, and PFUnDA can indicate a common exposure pathway to these long-chain PFCAs in humans.

The relationships between PFHxS and PFUnDA, PFOA and PFDA, and PFOA and PFUnDA were significant only in infants (SI Table S3). This finding further suggests the existence of unique sources of exposure to PFCs in infants such as breast milk and placental transfer.

Modeling of Daily Intake of PFCs Based on Measured Blood Concentrations. Based on the measured concentrations of blood PFC levels in adults, the daily intake of PFOS and PFOA were estimated by using a one-compartment toxicokinetic model (SI Table S4). The median concentrations of PFOS and PFOA in blood from Chinese adults were 7.75 and 0.79 ng/mL for male, and 9.92 and 0.99 ng/mL for female, respectively; the modeled daily intakes of PFOS and PFOA were, respectively, 0.74 and 0.07 ng/kg b.w./day for male, 1.20 and 0.12 ng/kg b.w./day for female.

In our recent study (*5*), we calculated the daily intake of PFOS and PFOA for Chinese adults based on the PFC concentrations in diet (meat, meat product, eggs, drinking water, fish, and seafood), and indoor dust. The modeled daily intake of PFOS in the present study were similar to the calculated daily intake via diet and indoor dust (0.74 vs 1.19 ng/kg b.w. for male, 1.20 vs 1.15 ng/kg b.w. for female), suggesting that dietary and indoor dust ingestion are the major exposure routes to PFOS for adults. However, for PFOA, the modeled daily intake (0.07−0.12 ng/kg b.w.) was much lower than the calculated daily intake via diet and indoor dust (9.55−9.85 ng/kg b.w.). The reason for the large difference between modeled and actual daily intake values for PFOA is unknown, but some input parameters for the one-compartment model have limitations. For example, half-life of PFOS and PFOA were derived only from a study of former fluorochemical company workers with a small sample size, mostly men (*26*). The one-compartment toxicokinetic model could not be used for infants, toddlers, children and adolescents because the input parameters were not available for these age groups.

Global Comparison of PFC Concentrations in Infants. The mean concentrations of PFCs in infants' blood from China, and from a few other countries are shown in SI Table S5. Concentrations of each of the PFCs in serum, from previous studies (*9, 14*), were converted into whole blood concentrations by dividing by a factor of 2 (*17*). In China, PFOS and PFOA were the predominant PFCs in infants, at mean concentrations of 4.20 ng/mL and 2.67 ng/mL, respectively, followed by PFNA, PFDA, PFUnDA, and PFHxS. (Table 1).

The concentrations of the detected PFCs in Chinese infants are relatively higher than those reported for infants from Australia (*9*), Norway (*14*), and the U.S. (*18*) (SI Table

S5). The concentrations of PFOS and PFOA in Chinese infants were similar to those reported in Australia (*9*), but were 2−4 times higher than those reported in Norway (*14*), and 3−5 times higher than those reported in the U.S. (*18*). PFNA and PFUnDA concentrations in Chinese infants were slightly higher than those reported for other countries (SI Table S5). High PFC concentrations in Chinese infants may be due to the increasing use of PFC-containing products by Chinese people with the increasing standard of living.

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Supporting Information Available

Additional information, figures, and tables as noted in text. This material is available free of charge via the Internet at http://pubs.acs.org.

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