Perchlorate and Iodide in Whole Blood Samples from Infants, Children, and Adults in Nanchang, China

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Perchlorate, ClO_4^-, interferes with iodide (I^-) uptake by the sodium-iodide symporter (NIS) and thereby affects thyroid hormone production in the body. Studies have reported human exposures to perchlorate based on measurements in urine, but little is known about the levels in blood. In this study, we determined concentrations of perchlorate, iodide, and other anions (e.g., chlorate [ClO_3^-], bromate [BrO_3^-], bromide [Br^-]) in 131 whole blood samples collected from Chinese donors aged 0.4 to 90 yr, in Nanchang, China. Perchlorate, iodide, and bromide were detected in all of the samples analyzed, whereas chlorate was found in only 27% of the samples and bromate was found in only 2%. The mean (range) concentrations of perchlorate, iodide, and bromide were 2.68 (0.51−10.5), 42.6 (1.58−812), and 2120 (1050−4850) ng/mL, respectively. Perchlorate levels in blood from Nanchang adults were 10-fold greater than levels that have been previously reported for U.S. adults. The iodide/perchlorate molar ratio ranged from 3.05 to 15.3 for all age groups, and the ratio increased with age ($r = 0.732$, $p < 0.01$). Perchlorate and bromide concentrations decreased significantly with age, whereas iodide concentrations increased with age. No significant gender-related differences in blood perchlorate, iodide, or bromide levels were found. A significant negative correlation was found between the concentrations of perchlorate and iodide in blood. Exposure doses of perchlorate were estimated for infants, toddlers, children, adolescents, and adults based on the measured concentrations in blood, using a simple pharmacokinetic model. The mean exposure doses of perchlorate for our age groups ranged from 1.12 (adults) to 2.22 μg/kg bw/day (infants), values higher than the United States Environmental Protection Agency's (USEPA) reference dose (RfD: 0.7 μg/kg bw/day). This is the first study on perchlorate and iodide levels in whole blood from infants, toddlers, children, adolescents, and adults from a city in China with known high perchlorate levels.

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Introduction

Perchlorate is a small anionic compound used as an oxidizing agent in rocket propellants, explosives, and fireworks (*1*). Perchlorate also occurs naturally in some fertilizers, and may be generated atmospherically (*2*). Since the early 1950s, the annual production of perchlorate in the U.S. has been estimated to be on the order of 4×10^8 kg, or an average production rate of 700 000 kg/yr (*3*). A combination of human activities and natural sources has led to the widespread presence of perchlorate in the environment (*4*−*6*), drinking water and foods (*7*−*10*), and in humans themselves (*11*−*13*).

Iodine (I_2) is an essential element required for the production of thyroid hormones, triiodothyronine (T3), and thyroxin (T4) in the thyroid gland. However, large doses (5.0 mg/kg bw/day) (*14*) of perchlorate can inhibit the uptake of iodide (I^-), thereby reducing the levels of these thyroid hormones in the body (*15*). Physiological levels of thyroid hormones are required for normal growth, brain development, and metabolic activities. Perchlorate has been reported to elicit developmental and neurobehavioral problems in infants and children (*16*). The toxic effect of perchlorate is exacerbated in individuals with low iodine intake in the diet (*14*).

Studies in the U.S. have shown that perchlorate and iodide are found in various human body fluids, such as urine (*17*, *18*), breast milk (*19*−*21*), amniotic fluid (*13*), saliva (*4*, *11*, *12*), and blood (*12*, *13*, *22*). Nevertheless, very few studies (*12*, *22*) have reported concomitant levels of perchlorate and iodide in human blood. Little is known on human exposures to perchlorate in China (*5*, *23*), although a recent study showed elevated levels of perchlorate in drinking water collected from several locations in China; such elevation is presumed to be related to the large scale production of fireworks. China is the largest producer of fireworks in the world. In this study, we determined perchlorate, iodide, and other anions, namely, chlorate [ClO_3^-], bromate [BrO_3^-], and bromide [Br^-], in whole blood sampled from 131 donors aged 0.4 to 90 yr. Perchlorate and iodide are highly soluble in water and can bind to blood proteins (*24*); these properties favor the choice of concentrations in blood as a measure of internal dose, and as an integrated measure of exposure from various sources.

Nanchang is the capital of Jiangxi Province, which has the second largest fireworks manufacturing operations in China. Based on the mean blood perchlorate concentrations that we measured for infants (0.4−1 yr), toddlers (1−5 yr), children (5−10 yr), adolescents (10−18 yr), and adults (18−90 yr), we estimated the daily intake of perchlorate for each age group, using a simple pharmacokinetic model developed earlier (*25*). Availability of samples from a wide range of age groups, with sufficient sample size, provided an opportunity to characterize the age- and gender-related accumulation of perchlorate, iodide, chlorate, bromate, and bromide in the general population in Nanchang. Ours is the first study to

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TABLE 1. Summary of Demographic Information of Blood Samples from Nanchang, China

age group (yrs)	no. of samples male	female	M + F[a]
infants			
0−1	4	5	9
toddlers			
1−2	7	2	9
2−3	5	4	9
3−4	8	5	13
4−5	4	3	7
children			
5−6	4	5	9
6−7	5	6	11
7−8	5	4	9
8−9	2	3	5
9−10	5	3	8
adolescents			
10−18	8	4	12
adults			
18−60	6	4	10
60−70	4	4	8
70−80	4	4	8
80−90	4	0	4
total	75	56	131

[a] M + F = males and females combined.

report the concentrations of perchlorate and iodide in human blood from China, especially for infants.

Materials and Methods

Chemicals and Devices. Ammonium perchlorate (>99.9%) and methylamine (40 wt % solution in water) were obtained from Sigma-Aldrich (St. Louis, MO). Chlorate and bromate standards were from APG (Belpre, OH). Sodium bromide and potassium iodide solutions (>99.5%) were from AccuStandard (New Haven, CT). Isotope-labeled sodium perchlorate ($Cl^{18}O_4^-$, >90%) was purchased from Cambridge Isotope Laboratories (Andover, MA). The Vivaspin 2 centrifugal filtration devices (CFDs) were obtained from Sartorius Stedim Biotech (Goettingen, Germany).

Sample Collection. The sampling area, Nanchang (28°38 N, 115°56 E), the capital of Jiangxi province located in southern China, is shown in Figure S1 (Supporting Information). The estimated population of the city in 2009 was 4 million. During February−March 2009, 131 blood samples were obtained from residents aged 0.4−90 yr. The blood samples were collected (2 mL) as part of routine clinical testing or for heavy metal (e.g., lead) analysis. The residual sample left after the clinical testing was used for perchlorate analysis. All participants lived in Nanchang, and were randomly selected. Therefore, our samples represent the general population of Nanchang. Participants' age, gender, and the date of blood collection were available for each sample, but information such as lifestyle, dietary habits, and occupation were not collected. The detailed demographic information including sample size, age, and gender is shown in Table 1. The participants' gender distribution was 57% male and 43% female. The overall age distribution was 7% infants ($n = 9$; 0.4−1 yr), 29% toddlers ($n = 38$; 1−5 yr), 32% children ($n = 42$; 5−10 yr), 9% adolescents ($n = 12$; 10−18 yr), and 23% adults ($n = 30$; 18−90 yr). All of the samples were stored in polypropylene containers at −20 °C until analysis. The blood collection was approved by the Institutional Review Board (IRB) of Nankai University, and the analysis was approved by the IRB of the New York State Department of Health.

Sample Preparation. Whole blood samples were thawed at room temperature and prepared immediately for analysis. Each blood sample (1 mL) was transferred to a Vivaspin 2 CFD. A 2-ng internal standard ($Cl^{18}O_4^-$; 200 μL, 0.01 ng/μL) and 800 μL of Milli-Q water were added. The diluted sample was vortexed to fully incorporate the internal standard in the sample matrix. The Vivaspin 2 CFD was centrifuged for 30 min at 4000*g*. The filtrate was transferred to sample vials and queued for analysis.

Instrumental Analysis. Samples were analyzed using an Agilent 1100 Series high-performance liquid chromatograph (HPLC; Agilent Technologies, Santa Clara, CA) coupled with a Micromass Quattro LC tandem mass spectrometer (MS/MS; Waters Corporation, Milford, MA), and injected using a Gilson 215 liquid handler (Gilson, Middleton, WI) and Gilson 819 injection module equipped a 100-μL injection loop. Data acquisition and calculation were accomplished with a Micromass MassLynx 3.5 (Waters Corporation). Separation of perchlorate, iodide, chlorate, bromate, and bromide in the blood sample was accomplished using an IonPac AS-21 column (guard column; 50 mm × 2 mm: regular column; 250 mm × 2 mm: Dionex, Sunnyvale, CA). The flow rate of the isocratic mobile phase, 200 mM methylamine water solution, was 0.3 mL/min. The injection volume was 100 μL; however, 150 μL was injected so as to completely fill the 100-μL sample loop. The perchlorate, chlorate, bromate, bromide, and iodide eluted at 6.0, 3.8, 3.5, 4.0, and 4.6 min, respectively, and total run time was 10 min.

Electrospray negative ionization (ESI$^-$) and multiple reaction monitoring (MRM) mode with the following mass transitions were used for identification and quantification of perchlorate, labeled-$Cl^{18}O_4^-$, chlorate, bromate, bromide, and iodide: 99 ($^{35}ClO_4^-$) > 83 ($^{35}ClO_3^-$), 101 ($^{37}ClO_4^-$) > 85 ($^{37}ClO_3^-$); 107 ($^{35}Cl^{18}O_4^-$) > 89 ($^{35}Cl^{18}O_3^-$); 83 ($^{35}ClO_3^-$) > 67 ($^{35}ClO_2^-$), 85 ($^{37}ClO_3^-$) > 69 ($^{37}ClO_2^-$); 127 ($^{79}BrO_3^-$) > 111 ($^{79}BrO_2^-$), 129 ($^{81}BrO_3^-$) > 113 ($^{81}BrO_2^-$); 79 ($^{79}Br^-$) > 79 ($^{79}Br^-$), 81 ($^{81}Br^-$) > 81 ($^{81}Br^-$); and 127 ($^{127}I^-$) > 127 ($^{127}I^-$). A relative response of native standard to isotopically labeled internal standard and the ratios of ^{35}Cl:^{37}Cl (for perchlorate and chlorate) and ^{79}Br: ^{81}Br (for bromate and bromide) were used for the confirmation of target analytes. The ratios were considered acceptable at 3.12 ± 25% for ^{35}Cl:^{37}Cl, and 1.03 ± 25% for ^{79}Br:^{81}Br. Further details of the instrumental method have been given elsewhere (*11, 12*).

Quality Assurance and Quality Control. Recoveries of perchlorate spiked into blood samples at 1 ($n = 5$) and 5 ng/mL ($n = 5$) levels, and passed through the entire analytical procedure were 83 ± 10% at 1 ng/mL level, and 92 ± 2% at 5 ng/mL level. The mean (±SD) recovery of internal standard ($Cl^{18}O_4^-$, $n = 131$) spiked into all of the samples was 100% (±8).

A 10-point calibration standard (in Milli-Q water) encompassing concentrations ranging from 0.01 to 100 ng/mL for perchlorate, 0.14 to 140 ng/mL for chlorate, 0.09 to 90 ng/mL for bromate, 0.05 to 500 ng/mL for bromide, and 0.02 to 200 ng/mL for iodide, was injected with each batch of 20 samples. The regression coefficient for calibration curves was >0.99 for all target analytes. Internal standard ($Cl^{18}O_4^-$) was spiked into each calibration standard and sample at 1 ng/mL. Over the course of analysis of the 131 blood samples, the average measured recoveries of calibration standards were 72%−106% of the theoretical concentrations for perchlorate, 77%−114% for chlorate, 92%−109% for bromate, 80%−105% for bromide, and 75%−124% for iodide. Along with every batch of samples, a laboratory reagent blank and an instrumental blank were analyzed; blood collection tubes were also checked for the presence of target anions analyzed in this study. Blanks contained trace levels of bromide and iodide, and reported concentrations in samples were subtracted from blanks. The limits of quantitation (LOQs)

TABLE 2. Perchlorate, Iodide, Chlorate, Bromate, and Bromide Concentrations (ng/mL) in Whole Blood from Infants, Toddlers, Children, Adolescents, and Adults from Nanchang, China

		perchlorate	chlorate	bromate	bromide	iodide
total ($n =$ 131)						
	detection[a] (%)	100	27	2	100	100
	mean (median)	2.68 (2.27)	0.44 (<0.30)	1.05 (<1.80)	2120 (2040)	42.6 (22.3)
	range	0.51−10.5	<0.30−3.80	<1.80−19.7	1050−4850	1.58−812
age group[b]						
infants ($n = 9$)	mean (median)	4.07 (3.33)	0.49 (<0.30)	<1.80	2470 (2320)	15.7 (15.0)
	range	2.16−8.63	<0.30−1.31	<1.80	1790−3320	12.5−21.7
toddlers ($n = 38$)	mean (median)	2.93 (2.54)	0.42 (<0.30)	0.92 (<1.80)	2210 (2030)	18.2 (15.9)
	range	1.26−10.5	<0.30−2.40	<1.80−1.82	1060−4850	1.58−69.8
children ($n = 42$)	mean (median)	2.56 (2.19)	0.56 (<0.30)	1.35 (<1.80)	2250 (2170)	27.7 (24.0)
	range	1.41−7.59	<0.30−2.75	<1.80−19.7	1410−4280	2.53−68.9
adolescents ($n = 12$)	mean (median)	2.51 (2.20)	0.57 (<0.30)	<1.80	2200 (2080)	25.2 (26.7)
	range	1.43−4.40	<0.30−3.80	<1.80	1430−3250	13.9−33.6
adults ($n = 30$)	mean (median)	2.18 (1.85)	0.25 (<0.30)	<1.80	1690 (1500)	110 (29.4)
	range	0.51−7.07	0.12−2.44	<1.80	1050−3600	14.1−812
gender						
male ($n = 76$)	mean (median)	2.71 (2.27)	0.50 (<0.30)	0.91 (<1.80)	2120 (2010)	42.2 (23.3)
	range	0.51−10.5	<0.30−2.75	<1.80−1.82	1050−4850	1.58−812
female ($n = 55$)	mean (median)	2.51 (2.43)	0.44 (<0.30)	1.20 (<1.80)	2040 (2110)	39.9 (21.7)
	range	0.71−8.63	<0.30−3.80	<0.18−19.7	1060−3340	2.53−450

[a] Detection = frequency of detection. [b] Age group including infants (0.4−1 yrs), toddlers (1−5 yrs), children (5−10 yrs), adolescents (10−18 yrs), and adults (18−90 yrs).

determined for perchlorate, chlorate, bromate, bromide, and iodide were 0.15, 0.3, 1.8, 20, and 0.5 ng/mL, respectively.

Statistical Analysis. Spearman's rank correlation was used to assess the relationship between subject's age and each of the anion concentrations, and between the concentration of perchlorate, iodide, and bromide; the differences in perchlorate, iodide, and bromide concentrations between males and females were evaluated using one-way analysis of variance (ANOVA). Concentrations below the LOQ were assigned half the value of the LOQ for statistical analysis. The data were analyzed with SPSS 17.0 (Chicago, IL).

Results and Discussion

Concentrations. Mean, median, and range concentrations of perchlorate, iodide, chlorate, bromate, and bromide in blood samples from Nanchang infants (0.4−1 yr), toddlers (1−5 yr), children (5−10 yr), adolescents (10−18 yr), and adults (18−90 yr) are shown in Table 2. Among the five anions analyzed, perchlorate, iodide, and bromide were found above the respective LOQs in 100% of the blood samples, whereas chlorate was detected only in 27% of the blood samples and bromate was detected in only 2% (Table 2). The results for chlorate and bromate are not discussed further. The mean (range) concentrations of perchlorate, iodide, and bromide in all blood samples were 2.68 (0.51−10.5), 42.6 (1.58−812), and 2120 (1050−4850) ng/mL, respectively (Table 2). Blood samples from infants contained the highest mean perchlorate (4.07 ng/mL) and bromide (2470 ng/mL) concentrations; these concentrations were approximately 2-fold greater than the concentrations found in adults' blood. The mean concentration of iodide (15.7 ng/mL) in blood from infants was 7-fold lower than the concentration in adults. Elevated concentrations of iodide were found in five of the blood samples from adults; these concentrations ranged from 305 to 812 ng/mL. This elevated concentration indicates that some individuals ingest large amounts of iodine from their diet. The five values appear to qualify as outliers, and were excluded from further discussions.

Very few studies have yet reported perchlorate and iodide levels in human blood. Oldi and Kannan (*12*) detected perchlorate in 82 human serum and plasma samples from adults in the U.S. and found a mean perchlorate concentration of 0.20 ng/mL. Blount et al. (*13*) reported a 50th percentile value of 0.22 ng/mL for perchlorate in 132 maternal serum samples collected in the U.S. In addition, that study found iodide in maternal serum samples at a mean concentration of 2.58 ng/mL (*13*). Perchlorate levels in human serum from Israel were reported to be 5.99, 1.19, and 0.44 ng/mL for high, medium, and low exposure groups, respectively (*22*). The mean perchlorate concentration in the blood samples from our Nanchang adults was similar to that reported for Israel, but was 10-fold greater than the concentration previously reported for adult human serum from the U.S. The sampling site (Jiangxi Province) has the second largest fireworks manufacturing operations in China. Furthermore, in Nanchang city, 300 tons of fireworks trash was generated in 2010 during the 7-day Chinese new year celebration. The manufacture and exhibition of fireworks in China are notable sources of perchlorate in the environment. A recent study found high levels of perchlorate in drinking water from Nanchang (*5*). In the U.S., diet has been reported as an important source of perchlorate exposure in humans (*7*−*10*). So, further studies are needed to evaluate perchlorate levels in foodstuffs from China.

The mean concentration of iodide in the blood of adult females from Nanchang (34.4 ng/mL) was 13-fold greater than the mean concentration (2.58 ng/mL) previously reported for maternal serum from the U.S (*13*). It should be noted that whole blood was analyzed in our study whereas serum was analyzed for the U.S. study. Thus, any comparison of perchlorate and iodide concentrations between these two countries must take into account the matrix differences. China was formerly an iodine-deficient country, with 40% of the world's iodine-deficient population. Therefore, the Chinese government implemented a program of distribution of iodized salt in 1994, with the aim of eliminating iodine deficiency by 2010, and this is a reason for the high iodide levels found in Chinese blood.

Perchlorate can competitively inhibit iodide uptake by the NIS (*26*). Therefore, concurrent quantification of iodide and perchlorate levels in human blood can provide information on potential risks from perchlorate exposures. The mean iodide concentration (24.2 ng/mL, after the exclusion of five outliers) in blood from Nanchang subjects was significantly

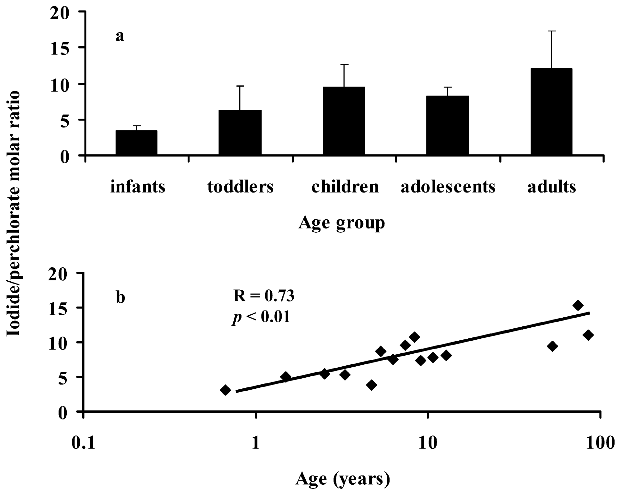

FIGURE 1. Molar ratio of iodide/perchlorate in blood (a) from various age groups, and (b) its relationship with age.

higher ($p < 0.01$) than the mean perchlorate concentration (2.68 ng/mL). The iodide/perchlorate molar ratio ranged from 3.05 (infants; 0.4−1 yr) to 15.3 (18−90 yr) (Figure 1a), and the ratio significantly increased with age ($r = 0.732$, $p < 0.01$) (Figure 1b); this increasing trend with age can be related to differences in pharmacokinetics, including daily dosage per unit body weight. Perchlorate has a 30-fold higher affinity for the NIS than does iodide (*26*). Although iodide levels are higher than perchlorate levels in most of the blood samples, four individuals had higher perchlorate concentrations than iodide concentrations in blood (perchlorate vs iodide: 2.60 vs 1.97; 2.70 vs 2.51; 3.40 vs 1.58; 4.15 vs 2.53 ng/mL, respectively); those individuals may be at high risk from the effects of perchlorate on thyroid hormone levels. However, it is worth noting that perchlorate and iodide are nonpersistent compounds in humans, and their levels in blood change depending on their intake and excretion. The effects of perchlorate on thyroid hormone levels are expected to occur at high and continuous exposures for an extended period of time. Further studies should analyze thyroid hormone levels in the samples that show such a pattern of [perchlorate] > [iodide] in blood.

Pregnant women, fetuses, and infants are particularly sensitive to the health effects of perchlorate exposure (*24*). In the present study, perchlorate concentrations in the whole blood of nine infants were in the range of 2.99−8.63 ng/mL, 2−6 times lower than the respective iodide concentrations. Bount et al. (*13*) found measurable concentrations of perchlorate in amniotic fluid and in cord-blood serum samples; infants can also be exposed to perchlorate via ingestion of breast milk (*19*−*21*, *27*).

Gender- and Age-Related Accumulation. Differences in the concentrations of perchlorate, bromide, and iodide were examined between males and females for each age group (Figure 2); no significant gender difference in concentrations of perchlorate, bromide, and iodide was found, for any age group.

The large size of the sample set ($n = 131$) and sampling across a wide age range (0.4−90 yr) enabled examination of age-related accumulation of perchlorate, bromide, and iodide in humans. Correlations between age and concentrations of the three anions were evaluated by Spearman's rank analysis (Figure 3). A significant decrease in perchlorate ($r = -0.319$, $p < 0.001$) (Figure 3a) and bromide ($r = -0.349$, $p < 0.001$) (Figure 3b) concentrations with age was found. However, concentrations of iodide ($r = 0.502$, $p < 0.001$) exhibited a significant positive correlation with age (Figure 3c). Similarly, a previous study (*28*) reported significantly higher concentrations of urinary perchlorate in children and adolescents

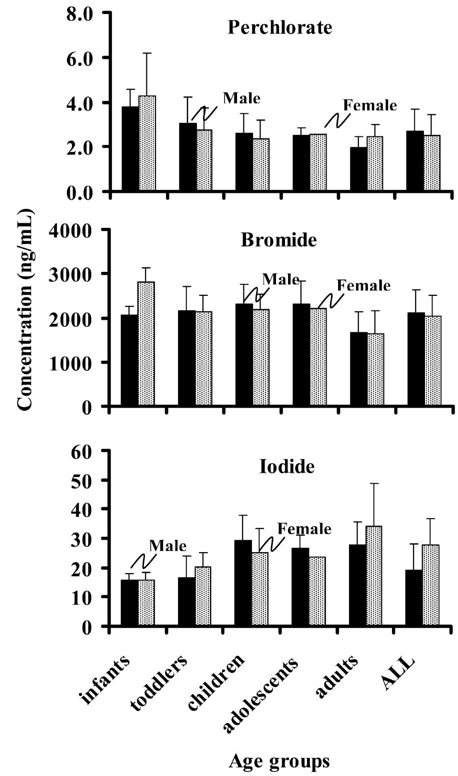

FIGURE 2. Mean concentrations of perchlorate, bromide, and iodide (ng/mL) in whole blood from male and female donors from the five age groups. Values below the LOQs were assigned ½ LOQ value.

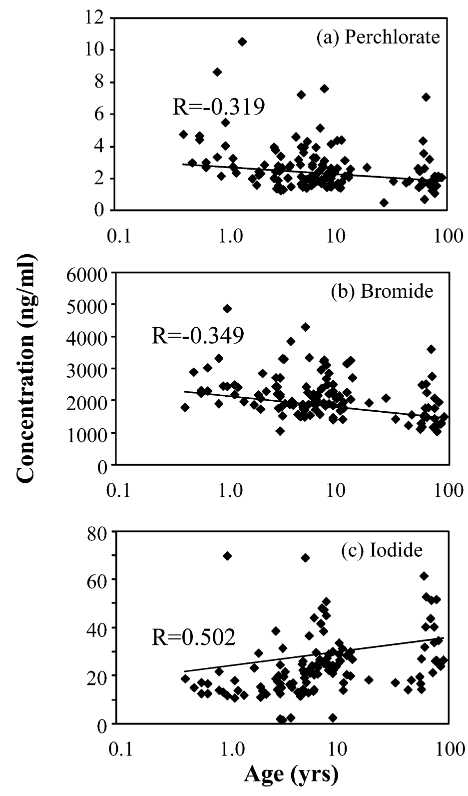

FIGURE 3. Relationship of perchlorate, bromide, and iodide concentrations (ng/mL) in blood with age of donors from Nanchang, China (five outlier values for iodide concentrations were excluded).

than in adults from the U.S. Furthermore, a significant positive correlation between iodide content in breast milk

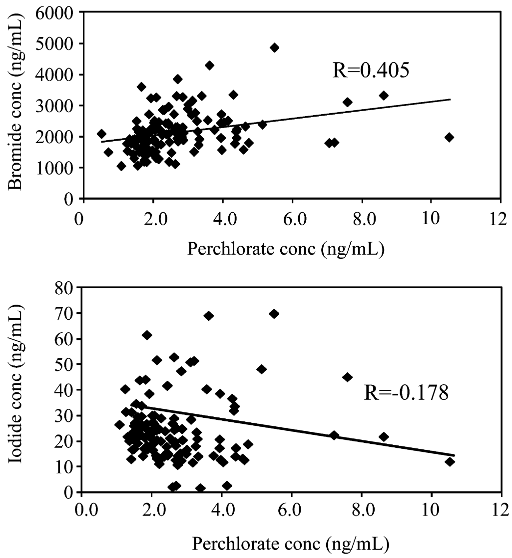

FIGURE 4. Relationship between perchlorate and bromide or iodide concentrations (ng/mL) in whole blood of donors from Nanchang, China (five outlier values for iodide concentrations were excluded).

and age was found for lactating women in Boston, MA, in the U.S (*20*). Age-related accumulation of blood perchlorate, bromide, and iodide may be due to the differences in dietary sources of exposure and pharmacokinetics. For instance, infants and children have the highest intakes of perchlorate, per unit body mass (*7*), due to consumption of breast milk and dairy foods (e.g., butter, milk, cheese, and ice cream), which contain high levels of perchlorate in the U.S. The manufacture and exhibition of fireworks may release perchlorate dust into environment (*29*). As we mentioned, our sampling site has the second largest firework manufacturing operation in China. The negative relationship between age and perchlorate levels may be due to high perchlorate exposure in infants and children via dust ingestion (*30*). However, high levels of iodide in adults are due to intake of more iodine-containing food such as iodized salt, iodine-containing multivitamins (*20*), and seafood (*31*). Furthermore, 70−95% of perchlorate is excreted unaltered in the urine (*14, 32*). Poor urinary elimination of perchlorate has been suggested for infants and children (*33*).

Relationship among Perchlorate, Iodide, and Bromide. A significant positive correlation between blood perchlorate and bromide concentrations was found in the present study ($r = 0.405$, $p < 0.001$). This correlation suggests that the sources of human exposures to perchlorate and bromide are related (Figure 4) or common such as drinking water. Bromide and its oxidized form, bromate, can be found in drinking water, as some disinfectants such as calcium hypochlorite contain these anions as impurities; elevated levels of perchlorate were also found in drinking water in Nanchang (*5*). Perchlorate concentration in blood was negatively correlated with iodide concentration ($r = -0.178$, $p < 0.05$) (Figure 4). A similar pattern was found between the concentrations of perchlorate and iodide in breast milk from the U.S. (*19, 20*). The negative correlation between perchlorate and iodide suggests differences in the sources of exposures to perchlorate and iodide. Milk and milk products, drinking water, fruits, and vegetables were found to be the major sources of perchlorate in the U.S. (*7*); iodized salt and seafood are the main dietary sources of iodide. Another possible reason for the negative correlation between perchlorate and iodide could be the role of perchlorate in reducing blood iodide levels (*21*), however, this suggestion needs further investigation, although there is an evidence of inhibition from exposure models (*34*).

Estimated Perchlorate Exposures Based on Blood Levels. The perchlorate exposure dose for each age group (infants, toddlers, children, adolescents, and adults) was estimated based on the blood perchlorate concentrations, using the following equation, as developed by Gibbs (*25*):

$$\log E = \frac{\log\left(\frac{C}{99.5}\right) - 1.052}{0.9193}$$

where E is estimated exposure dose (mg/kg bw/day), and C is the blood perchlorate level (μg/L); 99.5 is the molar mass of perchlorate.

Exposure dose estimates for nonpersistent toxicants (such as perchlorate) when based on data from one compartment, may not represent typical exposures. Given the episodic and varied nature of perchlorate exposure and the relatively short half-life of perchlorate in the body (~8 h) (*35*), the levels of perchlorate in blood are likely to vary with time (*36*). Thus, distributions of exposure dose based on spot samples are most precise at the central tendency, and the extremes of the distribution are likely to be overly extended.

Based on our measured concentrations of perchlorate in whole blood, the mean (range) exposure dose of perchlorate was estimated, as shown in Table 3. The mean exposure dose for each of the five age groups ranged from 1.12 (adults) to 2.22 μg/kg bw/day (infants). The estimated exposure doses of perchlorate (Table 3) were lower than the provisional maximum tolerable daily intake (PMTDI: 10 μg/kg bw/day) (*37*), recommended by the World Health Organization, and Food and Agriculture Organization of the United Nations. However, these values are higher than the USEPA's reference dose (RfD: 0.7 μg/kg bw/day) (*38*), a dose estimated to be without appreciable risk of adverse effects during a lifetime of exposure. The estimated daily intakes of perchlorate in 94% of the subjects investigated in the present study were above the USEPA's RfD. This finding indicates that the population in Nanchang, China, is exposed to high levels of perchlorate.

In our earlier study (*5*), we found that mean perchlorate concentration in tap water samples from Nanchang was 8.44 ng/mL. Assuming a daily water consumption rate of 2 L (*39*), and an average body weight of 55 kg (*40*) for adults, the daily intake of perchlorate via tap water was estimated to be 0.31 μg/kg bw/day, for adults. Thus, water consumption is an important source of perchlorate exposure, contributing to 27% of the estimated total daily intake value from blood concentrations. In addition to water consumption, dust ingestion and diet are potential sources of exposure to perchlorate.

In summary, the results of the present study suggest that the concentrations of perchlorate in human blood from Nanchang, China are 10-fold greater than concentrations that have been reported for populations in the U.S. A significant negative correlation between perchlorate concentration in blood and age was found, whereas blood iodide

TABLE 3. Mean (Range) Estimated Exposure Dose (μg/kg bw/day) of Perchlorate for Each Age Group Based on Blood Perchlorate Level

	infants	toddlers	children	adolescents	adults
estimated dose	2.22 (1.11−5.02)	1.55 (0.62−6.21)	1.34 (0.69−4.36)	1.31 (0.71−2.41)	1.12 (0.23−4.04)

concentrations increased with age. No significant gender-related differences in perchlorate, iodide, or bromide concentrations in blood were found. The lack of positive association between perchlorate and iodide suggests that human exposure sources of these two anions are different. The mean value for exposure dose of perchlorate by infants, toddlers, children, adolescents, and adults, based on the blood perchlorate concentrations measured in this study, was higher than the USEPA's RfD, suggesting that the study population is exposed to high levels of perchlorate. Based on the calculation in our previous study that drinking water consumption contributes to 27% of the total perchlorate intake by adults, remediation measures should focus on sources of potable water and exposures through diet.

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Supporting Information Available

Map of the sampling locations. This material is available free of charge via the Internet at http://pubs.acs.org.

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