Association Among Serum Perfluoroalkyl Chemicals, Glucose Homeostasis, and Metabolic Syndrome in Adolescents and Adults

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OBJECTIVE — Perfluoroalkyl chemicals (PFCs) have been used worldwide in a variety of consumer products. The effect of PFCs on glucose homeostasis is not known.

RESEARCH DESIGN AND METHODS — We examined 474 adolescents and 969 adults with reliable serum measures of metabolic syndrome profile from the National Health and Nutrition Examination Survey 1999–2000 and 2003–2004.

RESULTS — In adolescents, increased serum perfluorononanoic acid (PFNA) concentrations were associated with hyperglycemia (odds ratio [OR] 3.16 [95% CI 1.39–7.16], $P < 0.05$). Increased serum PFNA concentrations also have favorable associations with serum HDL cholesterol (0.67 [0.45–0.99], $P < 0.05$). Overall, increased serum PFNA concentrations were inversely correlated with the prevalence of the metabolic syndrome (0.37 [0.21–0.64], $P < 0.005$). In adults, increased serum perfluorooctanoic acid concentrations were significantly associated with increased β-cell function (β coefficient 0.07 ± 0.03, $P < 0.05$). Increased serum perfluorooctane sulfate (PFOS) concentrations were associated with increased blood insulin (0.14 ± 0.05, $P < 0.01$), homeostasis model assessment of insulin resistance (0.14 ± 0.05, $P < 0.01$), and β-cell function (0.15 ± 0.05, $P < 0.01$). Serum PFOS concentrations were also unfavorably correlated with serum HDL cholesterol (OR 1.61 [95% CI 1.15–2.26], $P < 0.05$).

CONCLUSIONS — Serum PFCs were associated with glucose homeostasis and indicators of metabolic syndrome. Further clinical and animal studies are warranted to clarify putative causal relationships.

Diabetes Care 32:702–707, 2009

The perfluoroalkyl chemicals (PFCs) are a family of perfluorinated chemicals that consist of a carbon backbone typically 4–14 carbons in length and a charged functional moiety (1). PFCs have been used extensively since the 1950s in commercial applications, such as inclusion as a component in surfactants, lubricants, paper and textile coatings, polishes, food packaging, and fire-retardant foams (2). Some of these PFCs, including the most widely known examples, perfluorooctanoic acid (PFOA) and perfluorooctane sulfate (PFOS), persist in humans and the environment and have been detected worldwide in wildlife (2). The routes of human exposure to PFCs are currently being investigated. Possible exposure pathways that are being examined include drinking water, dust in homes, and food or migration from food packaging and cookware. Animal studies have shown that these compounds are well absorbed orally but are poorly eliminated; they are not metabolized and undergo extensive uptake from enterohepatic circulation and are distributed mainly to the serum, kidney, and liver (1). Although some PFCs have been voluntarily removed from the market by manufacturers, PFOA and PFOS and their derivatives are still produced commercially, and the potential risk to humans continues to be evaluated.

In animal studies, exposure to PFOS and PFOA is associated with adverse health effects, including carcinogenicity (3,4), hepatotoxicity (4,5), and developmental and reproductive toxicity (4). For humans, PFC exposure has been shown to be associated with certain types of cancers (6). Maternal exposure to PFOS and PFOA also has been linked to low birth weight (7).

The causal biochemical mechanisms leading to the adverse health outcomes after exposure to PFCs are largely unknown. However, recent studies using advanced technologies in genomics and bioinformatics have shown that several categories of genes are commonly altered by some PFCs including those for peroxisome proliferation, fatty acid metabolism, lipid transport, cholesterol synthesis, proteosome activation and proteolysis, cell communication, and inflammation (1). The agonistic properties of PFCs on peroxisome proliferator-activated receptors-α [PPAR-α] are well supported and are thought to be a major mechanism leading to PFC-mediated liver damage (8,9). Because activation of PPAR-α can decrease serum triglycerides, normalize LDL cholesterol, and increase HDL cholesterol, we hypothesized that PFCs might have favorable effects on lipid homeostasis and may also be associated with reduced insulin resistance, an improved serum lipid profile, and lower prevalence of the metabolic syndrome. The goal of the present study was to test this hypothesis by examining data from the National Health and Nutrition Examination Survey (NHANES) collected from 1999–2000 and 2003–2004.

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Received 3 October 2008 and accepted 17 December 2008.
Published ahead of print at http://care.diabetesjournals.org on 29 December 2008. DOI: 10.2337/dc08-1816.

RESEARCH DESIGN AND METHODS

— Data were from NHANES 1999–2000 and 2003–2004. The NHANES is a population-based survey designed to collect information on the health and nutrition of the U.S. household population and to obtain a representative sample of the noninstitutionalized civilian U.S. population. The survey data are released every 2 years. Detailed survey operations manuals, consent documents, and brochures of the NHANES 1999–2000 and 2003–2004 are available on the NHANES Web site (10).

We limited our analyses to the 3,685 participants at least 12 years of age who had a blood test for PFCs. Among these subjects, only 1,788 subjects had a morning examination and had fasting plasma glucose, insulin, and triglyceride data available. Of these 1,788 participants, we included the 1,443 subjects without missing data for further analyses.

Anthropometric and biochemical data

According to the statements on the NHANES Web site, data were collected at all study sites by trained personnel following standardized procedures. Sociodemographic information such as age, sex, race/ethnicity, education level, and household income was collected during the household interview. Alcohol intake was determined by the questionnaire ("in any one year, have you had at least 12 drinks of any type of alcohol beverage?") and was dichotomized. For adolescents, because there were too many missing data, alcohol intake was not entered for analysis. Smoking status was categorized as active smoker, former/passive smoker, and nonsmoker by the smoking questionnaire and serum cotinine levels as described previously (11). Laboratory measurements were performed in a mobile examination center. Weight and height were measured using standard methods and digitally recorded. Three and sometimes four blood pressure determinations were collected by a physician using a mercury sphygmomanometer. Blood pressure was measured in the right arm unless otherwise specified. Averaged systolic blood pressure (SBP) and diastolic blood pressure (DBP) were obtained. Blood specimens were processed locally and then stored and shipped to central laboratories for analysis. Levels of serum total cholesterol and triglycerides were measured enzymatically. Levels of HDL cholesterol were measured after precipitation of other lipoproteins on a Hitachi model 704 analyzer (Roche Diagnostics, Indianapolis, IN). Serum C-reactive protein (CRP) levels were measured by latex-enhanced nephelometry. Plasma insulin was determined by an immunoenzymometric assay. Insulin resistance status (homeostasis model assessment of insulin resistance [HOMA-IR]) and β-cell function were estimated by the updated homeostasis model assessment (HOMA2) (12).

Table 1—*Basic demography and serum concentrations of PFCs of the sample subjects*

	Unweighted no. adolescent/adult	Adolescents (≥12 years, <20 years)	Adults (20 years)
Age (years)	474/969	15.5 ± 0.2	46.2 ± 0.8
Sex (%)			
Male	266/476	56.6 ± 3.1	50.2 ± 1.7
Female	208/493	43.4 ± 3.1	49.8 ± 1.7
Race (%)			
Mexican American	182/273	11.7 ± 2.5	8.7 ± 1.7
Non-Hispanic white	123/510	71.7 ± 3.5	80.8 ± 2.5
Non-Hispanic black	169/186	16.6 ± 2.6	10.5 ± 1.7
Smoking (%)			
Active smoker	66/197	19.1 ± 2.1	25.3 ± 2.5
Former/passive smoker	246/144	49.6 ± 3.6	14.5 ± 1.4
Nonsmoker	162/628	31.4 ± 3.8	60.2 ± 2.5
Alcohol drinking status (%)			
≥12 drinks last year	—/659	N/A	73.3 ± 2.3
<12 drinks last year	—/310	N/A	26.7 ± 2.3
Annual household income (%)			
<$25,000	186/352	27.3 ± 3.1	25.2 ± 2.4
$25,000–55,000	163/320	33.8 ± 3.6	33.4 ± 2.7
>$55,000	125/297	38.9 ± 3.9	41.4 ± 2.2
Metabolic syndrome (%)	38/382	8.6 ± 2.1	36.2 ± 2.0
Waist (%)	124/786	26.4 ± 2.7	81.2 ± 1.8
Glucose (%)	35/212	7.3 ± 2.1	15.7 ± 1.5
HDL cholesterol (%)	96/313	23.8 ± 3.1	32.6 ± 2.3
Triglyceride (%)	86/364	21.8 ± 2.8	34.6 ± 2.2
Blood pressure (%)	49/470	8.3 ± 1.6	42.0 ± 2.2
Diabetes medication	0/79	0	4.8 ± 0.7
Hypertension medication	0/245	0	19.5 ± 1.5
Hyperlipidemia medication	0/118	0	9.7 ± 1.0
Log CRP (mg/dl)	474/969	−2.94 ± 0.07	−1.54 ± 0.05
Log insulin (pmol/l)	474/969	4.05 ± 0.04	3.99 ± 0.04
Log PFHS (ng/ml)	474/969	0.95 ± 0.10	0.60 ± 0.04
Log PFNA (ng/ml)	474/969	−0.35 ± 0.07	−0.21 ± 0.07
Log PFOA (ng/ml)	474/969	1.51 ± 0.05	1.48 ± 0.04
Log PFOS (ng/ml)	474/969	3.11 ± 0.05	3.19 ± 0.04

Data are means ± SEM unless indicated otherwise. N/A, no assessment.

Definition of metabolic syndrome

For subjects >18 years old, presence of the metabolic syndrome was calculated by sex as defined by the National Cholesterol Education Program Adult Treatment Panel III (13) guideline of presenting with at least three of the following qualifications: waist measurement >88 cm for women and >102 cm for men; serum triglycerides ≥1.69 mmol/l; serum HDL cholesterol <1.03 mmol/l in men and <1.29 mmol/l in women; SBP ≥130 mmHg or DBP ≥85 mmHg or a self-report of taking antihypertensive medications; and fasting glucose ≥6.10 mmol/l or a self-report of taking antihyperglycemic medications. To define the metabolic syndrome among the young participants aged between 12 and 17 years, we used a previously proposed modification of the definition proposed in the National Cholesterol Education Program Adult Treatment Panel III. The participants had to meet three of the following five criteria: serum concentration of triglycerides ≥1.24 mmol/l; HDL cholesterol ≤1.04 mmol/l; waist circumference more than or equal to the sex-specific 90th percen-

tile (14); glucose concentration ≥5.55 mmol/l or a self-report of taking antihyperglycemic medications (15), and SBP or DBP more than or equal to the age-, height-, and sex-specific 90th percentile or a self-report of taking antihypertensive medications (16).

Assessment of serum PFCs

As part of NHANES, serum samples of PFOA, PFOS, perfluorohexane sulfonic acid (PFHS), and perfluorononanoic acid (PFNA) were collected for analysis. The analytical method has been described in detail (17). In brief, without protein precipitation, only dilution with 0.1 M formic acid, 1 aliquot of 100 μl serum was injected into a commercial column switching system allowing for concentration of the analytes on a C18 solid-phase extraction column. This column was placed automatically in front of a C8 analytical high-performance liquid chromatography column for chromatographic separation of the analytes. Detection and quantification were done using negative-ion TurboIonSpray ionization tandem mass spectrometry. Isotope-labeled internal standards were used for quantification.

Statistics

Data are expressed as means ± SEM. Participants were divided into adolescents (12–20 years of age) and adult (>20 years of age) groups for analysis. The strength of the associations between concentrations of various serum PFCs and blood glucose, insulin, and HOMA-IR levels was tested using multiple linear regression models. Logistic regression analyses were conducted to examine the odds ratios (ORs) of metabolic syndrome (yes or no for having at least three components of metabolic syndrome) and its components (yes/no for that component) associated with a 1 unit increase in log PFCs. Log transformation was performed for variables with significant deviation from normal distribution before further analyses. For linear regression, we used an extended model approach for covariate adjustment: model 1 = age, sex, and race; model 2 = model 1 + health behaviors (smoking status, alcohol intake, and household income); and model 3 = model 2 + measurement data (waist measurement, CRP, and insulin/glucose/HOMA) + current medications (antihypertensive, antihyperglycemic, and antihyperlipidemic agents). For logistic regression, the models for adjustment were as follows: model 4 = age, sex, race, health behaviors (smoking status, alcohol intake and household income), measurement data (CRP and HOMA/insulin), and current medications (antihypertensive, antihyperglycemic, and antihyperlipidemic agents) and model 5 = model 4 + other components of the metabolic syndrome. $P < 0.05$ was considered statistically significant. To avoid "model-dependent association," the association was considered significant only when it remained statistically significant in all models. Sampling weights that account for unequal probabilities of selection, oversampling, and nonresponse were applied for all analyses using the Complex Sample Survey module of SPSS (version 13.0 for Windows XP; SPSS, Chicago, IL).

Table 2—*Linear regression coefficients with 1-unit increase in log PFCs in adolescents and adults*

	β coefficient			
	Log PFHS	Log PFNA	Log PFOA	Log PFOS
Adolescent				
Glucose				
Model 1	−0.02 ± 0.03	0.04 ± 0.04	−0.04 ± 0.05	−0.03 ± 0.06
Model 2	−0.02 ± 0.03	0.05 ± 0.05	−0.04 ± 0.05	−0.04 ± 0.06
Model 3	−0.01 ± 0.03	0.07 ± 0.04	−0.03 ± 0.05	−0.03 ± 0.06
Log insulin				
Model 1	0.02 ± 0.04	−0.09 ± 0.05	0.05 ± 0.08	0.06 ± 0.07
Model 2	0.03 ± 0.04	−0.10 ± 0.05	0.07 ± 0.09	0.07 ± 0.07
Model 3	0.06 ± 0.03	−0.10 ± 0.05*	0.08 ± 0.07	0.15 ± 0.08
Log HOMA-IR				
Model 1	0.02 ± 0.04	−0.09 ± 0.05	0.04 ± 0.08	0.05 ± 0.07
Model 2	0.02 ± 0.05	−0.09 ± 0.05	0.06 ± 0.09	0.07 ± 0.07
Model 3	0.05 ± 0.03	−0.08 ± 0.04	0.08 ± 0.05	0.15 ± 0.07
Log β-cell function				
Model 1	0.03 ± 0.04	−0.12 ± 0.07	0.06 ± 0.10	0.06 ± 0.08
Model 2	0.03 ± 0.04	−0.12 ± 0.06	0.08 ± 0.10	0.08 ± 0.08
Model 3	0.05 ± 0.03	−0.12 ± 0.06*	0.08 ± 0.08	0.13 ± 0.09
Adult				
Glucose				
Model 1	−0.07 ± 0.09	−0.05 ± 0.04	−0.11 ± 0.10	−0.03 ± 0.08
Model 2	−0.05 ± 0.09	−0.02 ± 0.05	−0.11 ± 0.11	−0.23 ± 0.09
Model 3	−0.02 ± 0.06	0.00 ± 0.04	−0.09 ± 0.08	−0.03 ± 0.07
Log insulin				
Model 1	−0.04 ± 0.05	−0.06 ± 0.04	0.08 ± 0.04	0.13 ± 0.05*
Model 2	−0.04 ± 0.05	−0.05 ± 0.04	0.08 ± 0.04	0.13 ± 0.05*
Model 3	0.01 ± 0.03	−0.04 ± 0.03	0.07 ± 0.03*	0.14 ± 0.05†
Log HOMA-IR				
Model 1	−0.05 ± 0.05	−0.06 ± 0.04	0.06 ± 0.05	0.12 ± 0.05*
Model 2	−0.04 ± 0.05	−0.06 ± 0.05	0.07 ± 0.05	0.12 ± 0.05*
Model 3	0.00 ± 0.04	−0.04 ± 0.04	0.06 ± 0.04	0.14 ± 0.05†
Log β-cell function				
Model 1	−0.02 ± 0.04	−0.05 ± 0.03	0.09 ± 0.04*	0.14 ± 0.06*
Model 2	−0.02 ± 0.04	−0.05 ± 0.04	0.09 ± 0.04*	0.14 ± 0.06*
Model 3	0.01 ± 0.03	−0.04 ± 0.03	0.07 ± 0.03*	0.15 ± 0.05†

Data are means ± SEM. *$P < 0.05$; †$P < 0.01$. Model 1 adjusted for age, sex, race; model 2 adjusted for model 1 + health behaviors (smoking status, alcohol intake, and household income); model 3 adjusted for model 2 + measurement data (waist circumference, CRP, and insulin/glucose/HOMA) + medications.

RESULTS — The basic demographic characteristics of the participants are summarized in Table 1. The study sample consisted of 474 adolescents (aged between 12 and 20 years) and 969 adults (age >20 years). The serum PFHS levels were significantly higher in adolescents than in adults (log PFHS ng/ml 0.95 ± 0.10 vs. 0.60 ± 0.04, respectively, $P < 0.001$), whereas the serum PFNA concentrations were lower in adolescents than in adults (log PFNA ng/ml −0.35 ± 0.07 vs. −0.21 ± 0.07, $P = 0.001$). The serum PFOA and PFOS concentrations were not different between these two groups.

The associations between the serum PFC levels and glucose homeostasis markers are shown in Table 2. In adoles-

Table 3—*ORs of metabolic syndrome and its components associated with 1-unit increase in log PFCs in adolescents and adults*

	Log PFHS	Log PFNA	Log PFOA	Log PFOS
Adolescent				
Metabolic syndrome				
Model 4	0.56 (0.22–1.45)	0.37 (0.21–0.64)‡	0.79 (0.30–2.12)	0.49 (0.18–1.30)
Metabolic syndrome waist				
Model 4	0.72 (0.48–1.09)	0.99 (0.59–1.63)	0.61 (0.32–1.13)	0.41 (0.21–0.83)*
Model 5	0.64 (0.45–0.91)*	1.09 (0.61–1.95)	0.58 (0.34–1.00)*	0.37 (0.16–0.82)*
Metabolic syndrome glucose				
Model 4	1.10 (0.46–2.62)	3.15 (1.39–7.12)*	0.46 (0.25–0.85)*	0.58 (0.31–1.10)
Model 5	0.98 (0.44–2.17)	3.16 (1.39–7.16)*	0.55 (0.24–1.25)	0.58 (0.28–1.14)
Metabolic syndrome HDL cholesterol				
Model 4	0.93 (0.58–1.47)	0.59 (0.42–0.83)†	1.20 (0.60–2.39)	0.89 (0.51–1.55)
Model 5	0.93 (0.60–1.43)	0.67 (0.45–0.99)*	1.50 (0.67–3.36)	1.38 (0.61–3.14)
Metabolic syndrome triglycerides				
Model 4	1.07 (0.76–1.52)	0.68 (0.40–1.15)	1.64 (0.72–3.73)	0.95 (0.50–1.80)
Model 5	1.08 (0.83–1.40)	0.71 (0.37–1.34)	1.15 (0.54–2.47)	0.78 (0.41–1.49)
Adult				
Metabolic syndrome				
Model 4	0.93 (0.73–1.19)	0.92 (0.69–1.24)	1.07 (0.73–1.57)	1.25 (0.86–1.82)
Metabolic syndrome waist				
Model 4	0.73 (0.53–0.99)*	1.25 (0.88–1.74)	0.95 (0.63–1.45)	0.89 (0.59–1.34)
Model 5	0.80 (0.58–1.10)	1.34 (0.93–1.92)	0.97 (0.65–1.46)	0.91 (0.59–1.41)
Metabolic syndrome glucose				
Model 4	0.79 (0.53–1.16)	0.81 (0.62–1.07)	0.89 (0.63–1.26)	0.83 (0.64–1.08)
Model 5	0.76 (0.54–1.07)	0.86 (0.66–1.12)	0.87 (0.61–1.26)	0.81 (0.62–1.05)
Metabolic syndrome HDL cholesterol				
Model 4	0.90 (0.69–1.18)	0.80 (0.65–0.99)*	1.14 (0.84–1.55)	1.47 (1.07–2.00)*
Model 5	1.00 (0.73–1.37)	0.81 (0.65–1.00)	1.22 (0.86–1.71)	1.61 (1.15–2.26)*
Metabolic syndrome triglycerides				
Model 4	0.80 (0.64–0.99)*	0.98 (0.82–1.16)	0.91 (0.69–1.20)	0.97 (0.73–1.27)
Model 5	0.78 (0.60–1.02)	0.99 (0.81–1.19)	0.86 (0.65–1.13)	0.86 (0.65–1.16)

Data are OR (95% CI). *$P < 0.05$; †$P < 0.01$; ‡$P < 0.005$. Model 4 adjusted for age, sex, race, health behaviors (smoking status, alcohol intake, and household income), measurement data (CRP and HOMA/insulin) and medications. Model 5 adjusted for model 4 + other components of the metabolic syndrome.

cents, increased serum PFNA concentrations were associated with decreased blood insulin (β coefficient −0.10 ± 0.05, $P < 0.05$) and β-cell function (−0.12 ± 0.06, $P < 0.05$) with borderline significance ($P = 0.05$–0.09 in all models and <0.05 in the final model). Other PFCs were not associated with the serum markers for glucose homeostasis. In adults, increased serum PFOA concentrations were significantly associated with increased β-cell function (β coefficient 0.07 ± 0.03, $P < 0.05$). Increased serum PFOS concentrations were also associated with increased blood insulin (0.14 ± 0.05, $P < 0.01$), HOMA-IR (0.14 ± 0.05, $P < 0.01$), and β-cell function (0.15 ± 0.05, $P < 0.01$).

The associations between the serum PFCs and the metabolic syndrome/metabolic syndrome components are summarized in Table 3. In adolescents, increased serum PFNA concentrations were associated with a lower prevalence of the metabolic syndrome (OR 0.37 [95% CI 0.21–0.64], $P < 0.005$) and HDL cholesterol below the metabolic syndrome criteria (0.67 [0.45–0.99], $P < 0.05$). Increased serum PFNA concentrations were also correlated with a higher prevalence of blood glucose above the metabolic syndrome definition (3.16 [1.39–7.16], $P < 0.05$). We also found that the serum PFOS (0.37 [0.16–0.82], $P < 0.05$) concentrations were inversely correlated with a lower prevalence of waist circumference than the metabolic syndrome definition. In adult subjects, among all the PFCs and metabolic syndrome components, only serum PFOS concentrations were associated with a higher prevalence of HDL cholesterol below the metabolic syndrome definition (1.61 [1.15–2.26], $P < 0.05$).

CONCLUSIONS — To our knowledge, this report is the first to systemically analyze the link among serum PFC concentration, glucose homeostasis, and the metabolic syndrome/metabolic syndrome components in a nationally representative sample. In this study, we showed that PFCs were differentially associated with glucose homeostasis in adolescents and adults. We should consider carefully the extrapolation and interpretation of data between laboratory animal studies and the corresponding biological effects (at high parts per million range) compared with general human populations (at low parts per billion range). We found that the concentrations reported for PFCs in the occupational studies have been 2 and 3 orders of magnitude higher than those measured in the general population. Although there were several studies regarding maternal exposure and child

development, worker's exposure, and health outcome, the relationship of serum PFC levels to medical diseases and laboratory abnormality in a nationally representative survey has never been explored. Our results might suggest that low-dose PFC exposure may have effects on glucose metabolism in the general population.

Our analysis showed that the serum PFOA and PFOS concentrations were not different between adolescents and adults. Unlike other lipophilic persistent pollutants that display increasing serum concentrations as individuals age, the lack of this general trend in PFOS and PFOA could be explained by intrauterine transfer, exposure early in life with ongoing exposures being much higher than earlier historical exposures, or a combination of these factors (18). In contrast, the mean concentrations of PFHS were higher for adolescents than for adults, as reported previously (2,19). The higher concentrations of PHFS in children and adolescents could be related to their increased contact with carpeted floors containing PFHS, which is used for specific postmarket carpet treatment applications (2,19).

We showed that in adolescents, increased serum PFNA concentrations were associated with decreased blood insulin, impaired β-cell function (borderline significance), and clinical hyperglycemia. On the other hand, we found that increased serum PFNA had a favorable correlation with serum HDL cholesterol. Overall, increased serum PFNA concentrations were inversely associated with the prevalence of metabolic syndrome in adolescents. In adults, serum PFOS concentrations were independently associated with increases in both blood insulin and insulin resistance status (HOMA-IR). Interestingly, both serum PFOA and PFOS were also positively correlated with β-cell function. The balance between increased insulin resistance and β-cell function has a neutral effect on blood glucose. Increased PFOS also showed an unfavorable association with serum HDL cholesterol in adults. Overall, the PFCs in the present study had neutral effects on the prevalence of the metabolic syndrome in adults.

There has been a great deal of progress in the last few years in understanding the toxicology and distribution of PFCs in the environment, in wildlife, and in humans. However, there is a paucity of information pertaining to many specific PFCs (1). Thus far, there are no published reports of either in vitro or in vivo data pertaining to effects of PFCs on glucose homeostasis. The underlying mechanisms of this linkage are unknown and might partially be related to peroxisome activation. The liver toxicity of PFOS and PFOA has been linked to their PPAR-α agonist property (8,9). PFNA also has been shown to be a strong peroxisomal β-oxidation inducer in animals (20,21). Fibrates, amphipathic carboxylic acids that activate PPAR-α, can decrease triglycerides, normalize the LDL cholesterol profile, and increase HDL cholesterol (22). However, our results are not entirely consistent with previous animal findings, suggesting alternative or even multiple pathways in association among PFCs, glucose, and lipid metabolism. For example, Luebker et al. (23) have demonstrated that both PFOS and PFOA can interfere with the binding affinity of liver fatty acid–binding protein in rodents. Interestingly, they also found that among the PFCs tested, PFOS exhibited the highest level of inhibition of liver fatty acid–binding protein, which might partially explain the unfavorable association between increased serum PFOS and HDL cholesterol.

Our study has several limitations. First, the cross-sectional design does not permit any causal inference. Second, because of missing data, drinking status was not included in our analyses of adolescents.

In summary, we present the first report of a relationship between serum PFCs, glucose homeostasis, and metabolic syndrome. Because PFCs have been widely used worldwide in a variety of consumer products, further longitudinal clinical and in vitro studies are urgently needed to elucidate the putative casual relationships between PFCs and metabolism.

Acknowledgments— No potential conflicts of interest relevant to this article were reported.

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