Association Between Urinary Bisphenol A Concentration and Obesity Prevalence in Children and Adolescents

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Context Bisphenol A (BPA), a manufactured chemical, is found in canned food, polycarbonate-bottled liquids, and other consumer products. In adults, elevated urinary BPA concentrations are associated with obesity and incident coronary artery disease. BPA exposure is plausibly linked to childhood obesity, but evidence is lacking to date.

Objective To examine associations between urinary BPA concentration and body mass outcomes in children.

Design, Setting, and Participants Cross-sectional analysis of a nationally representative subsample of 2838 participants aged 6 through 19 years randomly selected for measurement of urinary BPA concentration in the 2003-2008 National Health and Nutrition Examination Surveys.

Main Outcome Measures Body mass index (BMI), converted to sex- and age-standardized *z* scores and used to classify participants as overweight (BMI ≥85th percentile for age/sex) or obese (BMI ≥95th percentile).

Results Median urinary BPA concentration was 2.8 ng/mL (interquartile range, 1.5-5.6). Of the participants, 1047 (34.1% [SE, 1.5%]) were overweight and 590 (17.8% [SE, 1.3%]) were obese. Controlling for race/ethnicity, age, caregiver education, poverty to income ratio, sex, serum cotinine level, caloric intake, television watching, and urinary creatinine level, children in the lowest urinary BPA quartile had a lower estimated prevalence of obesity (10.3% [95% CI, 7.5%-13.1%]) than those in quartiles 2 (20.1% [95% CI, 14.5%-25.6%]), 3 (19.0% [95% CI, 13.7%-24.2%]), and 4 (22.3% [95% CI, 16.6%-27.9%]). Similar patterns of association were found in multivariable analyses examining the association between quartiled urinary BPA concentration and BMI *z* score and in analyses that examined the logarithm of urinary BPA concentration and the prevalence of obesity. Obesity was not associated with exposure to other environmental phenols commonly used in other consumer products, such as sunscreens and soaps. In stratified analysis, significant associations between urinary BPA concentrations and obesity were found among whites ($P < .001$) but not among blacks or Hispanics.

Conclusions Urinary BPA concentration was significantly associated with obesity in this cross-sectional study of children and adolescents. Explanations of the association cannot rule out the possibility that obese children ingest food with higher BPA content or have greater adipose stores of BPA.

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BISPHENOL A (BPA) IS USED TO manufacture polycarbonate resin and is a breakdown product of coatings that prevent metal corrosion in food and beverage containers.[1] In the US population, exposure is nearly ubiquitous, with 92.6% of persons 6 years or older identified in the 2003-2004 National Health and Nutrition Examination Survey (NHANES) as having detectable BPA levels in their urine.[2] A comprehensive, cross-sectional study of dust, indoor and outdoor air, and solid and liquid food in preschool-aged children[3] suggested that dietary sources constitute 99% of BPA exposure. BPA is rapidly excreted in urine, with a half-life in the range of 4 to 43 hours.[4,5] However, BPA also has been detected in fat,[6] and urinary BPA concentrations do not decline rapidly with fasting time, suggesting that the compound accumulates in fat and other physiologic compartments.[4]

In experimental studies, BPA exposure has been shown to disrupt multiple metabolic mechanisms,[7,8] suggesting that it may increase body mass in environmentally relevant doses[9,10] and therefore contribute to obesity in humans. This possibility has recently been explored in adults. One cross-sectional study found an association between urinary BPA concentration and increased risk of obesity in adults in the US population, using the NHANES.[11] Other studies have demonstrated associations between urinary BPA concentration and adult diabetes, cardiovascular diagnoses, and abnormalities in liver func-

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tion.[12,13] A longitudinal study of apparently healthy adults showed an association between baseline urinary BPA concentration and later-life coronary artery disease.[14]

The special vulnerability of children to environmental chemicals[15] amplifies concerns about BPA exposure in this population. Although obesity reflects individual behaviors, the built environment, and possibly synthetic chemical obesogens, prior studies have heavily emphasized the first 2 of these factors rather than the third.[16]

We therefore examined urinary BPA concentrations and body mass outcomes in 6- to 19-year-olds in the 2003-2008 NHANES.

METHODS

Data Source and Sample

The NHANES is a continuous, multicomponent, nationally representative survey of the noninstitutionalized US population administered by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention. We used information from the questionnaire, laboratory, diet, and physical examination components of the NHANES, for which data are available in biennial groupings. Urinary samples—the source for BPA concentration in this study—have been analyzed in a one-third subsample from the 2003-2004 survey forward; although BPA concentrations for 2009-2010 were available at the time of our analysis, dietary data were not.

Written consent, and child assent as appropriate, was obtained from parents/guardians or participants after approval by the NCHS research ethics review board. The New York University School of Medicine institutional review board exempted this study from review because it is based on previously collected data that have been deidentified.

Measurement of Urinary BPA Concentration

Urinary BPA concentration was measured in 1 spot sample from each participant and analyzed using high-performance liquid chromatography and tandem mass spectroscopy. More extensive methodological description is provided elsewhere.[17] For urinary BPA concentrations below the level of detection (100 [3.5%]), we substituted the value of 0.3 ng/mL routinely assigned by the NHANES. To correct for urinary dilution, we controlled for urinary creatinine in all multivariable models, following usual practice.[2,4] To assess possible systematic bias introduced by a change in the method used to measure urinary creatinine levels in 2007, we added a categorical variable representing NHANES wave to our final multivariable models as part of a sensitivity analysis.

Body Mass Outcomes

In the NHANES, trained health technicians assessed body measurements, following standardized procedures.[18] Body mass index (BMI), calculated as weight in kilograms divided by height in meters squared, was used to measure adiposity. Because BMI varies widely by age and sex, age- and sex-standardized BMI *z* scores are commonly used. These were derived using Centers for Disease Control and Prevention year 2000 norms. Overweight and obese were categorized as BMI *z* score of 1.036 or greater (85th percentile for age and sex) and 1.64 or greater (95th percentile), respectively.[19] Our primary study outcome was obesity, although we also examined overweight and BMI *z* score as secondary study outcomes.

Control for Potential Confounders

Trained interviewers fluent in Spanish and English elicited total 24-hour calorie intake in person, using standard measuring guides to assist reporting of volumes and dimensions of food items.[20] The physical activity variables changed during the study period, complicating the categorization of physical activity in children into low, medium, and high, as would be used to derive caloric needs using age- and sex-specific US Department of Agriculture guidelines.[21] As a conservative measure, we therefore assumed all participants to have high physical activity and categorized them as having "normal" and "excessive" caloric intake based on the daily caloric guidelines set for children with high physical activity, recognizing that this probably underestimates the extent to which some exceeded US Department of Agriculture calorie intake guidelines.

We used daily hours of television watching to assess behavioral risk (with a cut point of ≥2 h/d, in light of the previous association with obesity in NHANES).[22] Because exposure to tobacco smoke is a risk factor for the metabolic syndrome in adolescence,[23] we included serum cotinine level in multivariable models. We categorized it into low (<0.015 ng/mL), medium (≥0.015 to <2 ng/mL), and high (≥2 ng/mL) categories, following previous practices.[24]

Race/ethnicity was categorized into Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other, based on self-report by 17- to 19-year-olds and caregiver report in 6- to 16-year-olds. Caregiver education was categorized as less than 9th grade, 9th through 12th grade, high school/General Equivalency Diploma, some college, and college or greater. Poverty-income ratio was categorized into quartiles, within the sample for which urinary BPA concentration was measured. Age was categorized into 2 groups: 6 through 11 and 12 through 19 years.

To maximize sample size in multivariable analysis, "missing" categories were created for all potential confounders. Data on television watching were missing in 17.4% and on serum cotinine level in 11.1%. Otherwise, less than 5% of values were missing for any confounding variable. As a robustness check, we repeated our main multivariable analysis as a complete case analysis, omitting observations that had missing values for any of the covariates.

Statistical Analysis

Appropriately weighted univariable, bivariable, and multivariable analyses

were conducted in a fashion that reflects the NHANES complex survey sampling design, using Stata 12.0 and following NCHS guidelines.[25] All analyses applied 2-sided tests, using a cutoff of $P = .05$ for significance. Because overweight and obesity are highly prevalent in our sample, we present adjusted odds ratios (ORs) along with estimated prevalences (which incorporate the complex sample weighting), based on multivariable models.

We also created unweighted sample quartiles for urinary BPA concentration and used these indicator variables to further allow for nonlinearity in tests of association. We performed χ^2 analyses of the association between urinary BPA quartile and the potential confounders named above and with categorical overweight and obesity.

To assess heterogeneity of association in subpopulations, we also developed regression models of the association between urinary BPA concentrations and obesity, controlling for urinary creatinine level, in strata defined by each of the potential confounding categorical variables described previously. As a further test of heterogeneity, we added stratum × urinary BPA concentration interaction terms to whole-sample regression models controlling for urinary creatinine level to test those interactions for statistical significance. When interaction terms had $P < .05$, we interpreted this to confirm a stratum-specific effect.

Multivariable regression analysis was used to model BMI *z* score and logistic regression to model categorical overweight and obese. All initial models adjusted for urinary creatinine level, while final multivariable models also included race/ethnicity, age, caregiver education, poverty to income ratio, sex, serum cotinine level, and lifestyle characteristics (caloric intake and television watching). From the logistic models, we present adjusted ORs as well as estimated prevalences, which are probabilities calculated from the multivariable logistic models, including survey sampling weights and design. As an additional analysis, to investigate linearity of associations between urinary BPA concentrations and body mass, we reiterated all regression analyses substituting the logarithm of the urinary BPA concentration for quartiled concentrations. The log transformation was necessary because of the skewed distribution of urinary BPA concentrations in the study population.

Analysis for Specificity of Association

We also examined associations of urinary concentrations of several environmental phenols that are chemically similar to BPA and that were measured in the NHANES. Benzophenone-3 is widely used in sunscreens, 4-tertoctylphenol is used in detergents and other industrial cleaners, and triclosan is present in soaps, deodorants, shaving creams, and toothpastes.[26] These phenols are not routinely used in food packaging or aluminum can linings.

Urinary concentrations were categorized into quartiles (or in the case of 4-tertoctylphenol into detectable/nondetectable) and examined for their association with indicators of body mass/obesity, adjusting for urinary creatinine level. Quartiles of these other phenols were also added individually to the final multivariable models, with obesity as an outcome.

RESULTS

During the study period (2003-2008), 9270 children and adolescents aged 6 through 19 years participated in NHANES. Our analytic sample comprised the 2838 nonpregnant participants randomly selected for measurement of urinary BPA concentrations. Median urinary BPA concentration was 2.8 ng/mL (interquartile range, 1.5-5.6).

TABLE 1 presents descriptive and bivariate analyses of urinary BPA quartile with demographic, environmental, dietary, and physical activity covariates as well as primary study outcomes. Within the subsample, prevalence of obesity (590 [17.8%]) and overweight (1047 [34.1%]) were consistent with other reports from NHANES 2003-2008.[27] As previously noted in analysis of the 2003-2004 NHANES sample,[2] distributions of urinary BPA concentrations differed by race/ethnicity, with a preponderance of lower concentrations in Mexican Americans and higher concentrations in non-Hispanic blacks. Concentrations were also lowest among children with caregivers at both educational extremes. Children with the lowest serum cotinine levels (<0.015 ng/mL) had a preponderance of lower urinary BPA concentrations. Caloric intake and television watching were not significantly associated with urinary BPA quartiles, but quartile was associated with overweight and obesity.

Association of Urinary BPA Concentration With Obesity

TABLE 2 examines associations between urinary BPA concentration quartile and obesity from logistic regression models, controlling for urinary creatinine level. In the whole population, the odds of obesity were increased in the second (OR, 2.22 [95% CI, 1.53-3.23]), third (OR, 2.09 [95% CI, 1.48-2.95]), and fourth (OR, 2.53 [95% CI, 1.72-3.74]) quartiles of urinary BPA concentration ($P < .001$ for all estimates). Corresponding estimated prevalences were 10.0% (95% CI, 7.6%-12.5%) for the first quartile, 19.9% (95% CI, 15.0%-24.7%) for the second, 18.9% (95% CI, 14.8%-23.0%) for the third, and 22.1% (95% CI, 17.0%-27.2%) for the fourth.

Further stratified analyses showed this association to be statistically significant in only 1 racial subpopulation. Although the risk for whites beyond the first quartile was substantial (second quartile: OR, 4.32 [95% CI, 2.08-8.99]; third quartile: OR, 4.20 [95% CI, 2.01-8.77]; fourth quartile: OR, 6.03 [95% CI, 2.88-12.62]; $P < .001$ for all estimates; estimated prevalences, 4.7% [95% CI, 1.8%-7.6%], 17.5% [95% CI, 0.6%-24.4%], 17.1% [95% CI, 11.7%-22.4%], and 22.8% [95% CI, 15.8%-29.8%], respectively, in increasing quartiles), neither Hispanic (Mexican American and other Hispanic) or non-Hispanic black chil-

dren had a significantly increased risk of obesity with elevated concentrations of urinary BPA. Whole-sample statistical analysis of the race/ethnicity-urinary BPA quartile interaction with obesity as the outcome showed significant interactions for white participants (second-quartile OR, 3.10 [95% CI, 1.33-7.21; P=.01]; third-quartile OR, 3.33 [95% CI, 1.48-7.49; P=.005]; fourth-quartile OR, 4.08 [95% CI, 1.66-10.0; P=.003]) and no significant association for participants of other races/ethnicities. Further whole-sample analysis of the race/ethnicity–urinary BPA concentration interaction with BMI z score failed to confirm a significant

Table 1. Study Population Characteristics in Urinary Bisphenol A Quartiles in Pooled 2003-2008 NHANES (N = 2838)

Characteristic	All		Urinary Bisphenol A Concentration Quartile, % (SE)[a]				P Value[c]
	No.	% (SE)[b]	1 (n = 685)	2 (n = 700)	3 (n = 737)	4 (n = 716)	
Sex							
Female	1374	48.7 (1.3)[d]	48.9 (2.5)	50.9 (2.5)	47.0 (3.2)	47.3 (2.5)	.74
Male	1464	51.3 (1.3)	51.1 (2.5)	49.1 (2.5)	53.0 (3.2)	52.7 (2.5)	
Age group, y							
6-11	1059	42.0 (1.3)	42.1 (2.1)	40.7 (2.3)	43.7 (2.7)	42.2 (2.5)	.84
12-19	1779	58.0 (1.3)	57.9 (2.1)	59.3 (2.3)	56.3 (2.7)	57.8 (2.5)	
Race/ethnicity							
Hispanic–Mexican American	850	12.2 (1.3)	16.3 (1.9)	13.8 (1.6)	10.4 (1.5)	9.0 (1.3)	<.001
Hispanic–other Hispanic	162	4.6 (0.9)	5.2 (1.4)	6.3 (1.3)	4.1 (1.3)	2.9 (0.9)	
Non-Hispanic white	789	62.0 (2.5)	59.4 (3.4)	60.7 (2.7)	64.7 (3.6)	62.3 (3.1)	
Non-Hispanic black	903	14.9 (1.4)	10.9 (1.7)	13.6 (1.6)	16.9 (2.0)	18.5 (2.1)	
Other	134	6.3 (0.9)	8.1 (1.7)	5.5 (1.2)	3.9 (1.0)	7.2 (1.5)	
Poverty to income ratio quartile							
1 (<0.83)	658	16.5 (1.3)	15.8 (2.0)	14.1 (1.7)	17.7 (1.8)	17.6 (1.8)	.09
2 (0.83-1.59)	691	18.5 (1.3)	15.3 (1.5)	18.9 (2.2)	19.5 (1.9)	20.7 (2.2)	
3 (1.60-3.09)	671	25.3 (1.4)	22.0 (2.6)	25.5 (2.6)	25.8 (2.3)	28.0 (2.2)	
4 (≥3.1)	678	35.8 (2.5)	42.4 (3.0)	37.6 (3.6)	33.3 (2.9)	30.2 (3.8)	
Missing	140	4.0 (0.5)	4.6 (1.1)	3.8 (0.9)	3.7 (1.0)	3.5 (0.6)	
Caregiver education							
<9th grade	334	6.5 (0.6)	8.1 (1.3)	6.6 (1.1)	4.9 (0.7)	6.3 (0.6)	.046
9th-12th grade	538	13.0 (1.1)	10.6 (1.5)	13.1 (1.8)	13.8 (1.7)	14.6 (1.8)	
High school or GED	641	23.1 (1.2)	19.8 (1.7)	21.4 (2.4)	25.9 (2.4)	26.1 (1.9)	
Some college	784	31.2 (1.3)	29.1 (2.5)	30.9 (2.3)	34.1 (2.7)	30.4 (2.5)	
College or greater	417	22.5 (1.8)	26.9 (3.2)	25.1 (2.9)	18.5 (2.0)	19.4 (2.6)	
Missing	124	3.8 (0.5)	5.6 (1.3)	3.0 (1.0)	3.2 (0.8)	3.2 (0.9)	
Serum cotinine, ng/mL							
<0.015	442	14.8 (1.5)	19.2 (2.6)	18.7 (1.8)	12.3 (2.0)	9.6 (1.7)	<.001
0.015-1.9	1706	59.0 (1.4)	56.9 (3.3)	58.5 (2.4)	62.3 (2.5)	57.4 (2.6)	
≥2.0	375	14.5 (1.1)	14.0 (2.3)	10.4 (1.5)	13.3 (1.6)	19.8 (2.2)	
Missing	315	11.7 (0.8)	9.8 (1.7)	12.4 (1.7)	12.1 (1.5)	13.3 (1.6)	
Television watching, h/d							
<2	744	35.2 (1.4)	38.7 (2.7)	32.4 (2.7)	33.5 (2.4)	36.8 (2.9)	.30
≥2	1599	64.8 (1.4)	61.3 (2.7)	67.6 (2.7)	66.5 (2.4)	63.2 (2.9)	
Caloric intake vs active child of same age and sex[e]							
>USDA cut point	802	29.7 (1.3)	30.7 (2.5)	31.2 (2.6)	30.3 (2.1)	26.1 (2.0)	.34
≤USDA cut point	1898	70.3 (1.3)	69.3 (2.5)	68.8 (2.6)	69.7 (2.1)	73.9 (2.0)	
Overweight							
No	1769	65.9 (1.5)	71.5 (2.2)	65.7 (2.7)	63.4 (2.6)	63.5 (2.9)	.08
Yes	1047	34.1 (1.5)	28.5 (2.3)	34.3 (2.7)	36.6 (2.6)	36.5 (2.9)	
Obese							
No	2226	82.2 (1.3)	90.2 (1.2)	80.1 (2.5)	80.9 (2.1)	77.5 (2.5)	<.001
Yes	590	17.8 (1.3)	9.8 (1.2)	19.9 (2.5)	19.1 (2.1)	22.5 (2.5)	

Abbreviations: GED, General Equivalency Diploma; NHANES, National Health and Nutrition Examination Survey; USDA, United States Department of Agriculture.
[a] Quartile 1: urinary bisphenol A concentrations <1.5 ng/mL; quartile 2: 1.5-2.7 ng/mL; quartile 3: 2.8-5.5 ng/mL; quartile 4, ≥5.6 ng/mL.
[b] All percentages are weighted using population weights for the sample in which bisphenol A concentration was measured.
[c] Calculated using a χ^2 test.
[d] Total number of participants for some variables do not total to 2838 because of missing data. See "Methods."
[e] USDA cut point indicates cut point for children with high physical activity.

Table 2. Association of Urinary Bisphenol A Concentration and Odds and Prevalence of Obesity in Strata Defined by Sample Characteristics[a]

	All		Urinary Bisphenol A Concentration Quartile[b]						
			1 (n = 685)	2 (n = 700)		3 (n = 737)		4 (n = 716)	
	Unweighted No., Obese/Total	Obese in Stratum, % (SE)[c]	Prevalence (95% CI), %	OR (95% CI)	Prevalence (95% CI), %	OR (95% CI)	Prevalence (95% CI), %	OR (95% CI)	Prevalence (95% CI), %
Entire sample	590/2816	17.8 (1.3)	10.0 (7.6-12.5)	2.22 (1.53-3.23)[d]	19.9 (15.0-24.7)	2.09 (1.48-2.95)[d]	18.9 (14.8-23.0)	2.53 (1.72-3.74)[d]	22.1 (17.0-27.2)
Sex									
Female	285/1366	16.5 (1.5)	10.8 (6.7-14.8)	1.86 (1.10-3.17)[e]	18.4 (12.4 to 24.3)	1.65 (0.93-2.92)	16.6 (11.6-21.6)	2.00 (1.15-3.49)[e]	19.5 (13.5-25.5)
Male	305/1450	19.0 (1.8)	9.4 (6.5-12.4)	2.63 (1.56-4.43)[d]	21.6 (15.2-27.9)	2.56 (1.66-3.96)[d]	21.1 (15.2-27.0)	3.14 (1.79-5.48)[d]	24.7 (17.2-32.1)
Age group, y									
<12	227/1055	18.0 (1.6)	12.2 (6.8-17.5)	1.72 (1.05-2.81)[e]	19.2 (11.7-26.6)	1.91 (1.14-3.21)[e]	20.9 (15.1-26.6)	2.34 (1.31-4.18)[e]	24.3 (18.1-30.5)
≥12	363/1761	17.6 (1.5)	9.6 (6.1-13.1)	2.59 (1.49-4.48)[f]	21.6 (15.7-27.5)	2.14 (1.25-3.64)[f]	18.6 (13.3-23.8)	2.57 (1.55-4.23)[f]	21.5 (15.3-27.6)
Race/ethnicity									
Hispanic	227/1004	23.2 (1.9)	22.4 (17.2-27.6)	1.24 (0.80-1.92)	26.5 (20.2-32.7)	0.94 (0.58-1.49)	21.3 (14.9-27.7)	1.02 (0.65-1.59)	22.8 (16.0-29.7)
Non-Hispanic white	124/787	15.5 (1.7)	4.7 (1.8-7.6)	4.32 (2.08-8.99)[d]	17.5 (10.6-24.4)	4.21 (2.01-8.77)[d]	17.1 (11.7-22.4)	6.03 (2.88-12.62)[d]	22.8 (15.8-29.8)
Non-Hispanic black	216/893	24.5 (1.9)	20.8 (13.8-27.9)	0.99 (0.58-1.66)	20.7 (15.2-26.2)	1.38 (0.78-2.47)	26.8 (19.2-34.3)	1.34 (0.75-2.38)	26.1 (18.3-33.8)
Other	23/132	10.3 (2.9)	7.1 (–2.4 to 16.7)	2.84 (0.64-12.4)	17.7 (3.8-31.7)	2.11 (0.30-14.8)	13.9 (0.5-27.3)	1.22 (0.25-5.86)	8.6 (2.5-14.6)
Poverty to income ratio									
<1.6	305/1335	22.5 (1.8)	15.1 (10.6-19.7)	2.22 (1.46-3.35)[d]	28.3 (20.8-35.9)	1.70 (1.04-2.78)[e]	23.3 (17.8-28.8]	1.54 (0.93-2.55)	21.6 (16.9-26.4]
≥1.6	254/1343	15.4 (1.4)	7.7 (4.6-10.8)	2.22 (1.28-3.86)[f]	15.7 (11.3-20.0)	2.26 (1.32-3.88)[f]	15.9 (10.8-21.05)	3.62 (1.96-6.68)[d]	23.2 (15.9-30.5)
Missing	31/138	14.2 (3.4)	9.3 (0.09-18.5)	2.08 (0.35-12.01)	17.4 (1.3-33.5)	3.24 (0.80-13.16)	24.6 (7.2-41.9)	1.17 (0.26-5.19)	10.7 (1.7-19.6)
Caregiver education[g]									
Less educated	366/1497	22.4 (1.9)	12.8 (8.7-16.9)	2.09 (1.26-3.47)[f]	23.5 (16.8-30.1)	1.92 (1.17-3.17)[e]	22.0 (15.9-28.2)	2.78 (1.61-4.77)[f]	28.9 (21.6-36.3)
More educated	201/1196	14.2 (1.3)	7.6 (3.8-11.3)	2.60 (1.33-5.10)[f]	17.6 (12.1-23.1)	2.31 (1.21-4.38)[e]	15.9 (11.2-20.6)	2.31 (1.20-4.46)[e]	15.9 (10.5-21.4)
Missing	23/123	17.8 (4.4)	17.5 (–0.1 to 35.1)	0.84 (0.12-5.88)	15.0 (–3.1 to 33.1)	1.58 (0.24-10.00)	25.0 (4.6-45.4)	0.87 (0.15-5.09)	15.6 (1.2-30.0)
Serum cotinine									
<2 ng/mL	454/2134	17.6 (1.5)	11.1 (8.0-14.3)	2.24 (1.47-3.40)[d]	21.9 (16.3-27.4)	1.50 (1.04-2.16)[e]	15.9 (11.9-19.9)	2.19 (1.44-3.31)[d]	21.5 (16.2-26.8)
≥2 ng/mL	73/372	18.8 (2.6)	5.0 (0.0-10.3)	3.38 (0.85-13.34)	14.9 (4.5-25.4)	10.93 (2.24-53.20)[f]	35.9 (20.4-51.4)	6.50 (1.36-31.00)[e]	25.1 (12.3-37.9)
Missing	63/310	17.8 (3.0)	11.2 (1.8-20.7)	1.16 (0.31-4.40)	12.9 (3.5-22.2)	2.29 (0.68-7.73)	22.5 (10.7-34.2)	2.37 (0.63-8.80)	23.1 (9.2-36.9)
Television watching									
<2 h/d	227/1224	15.5 (1.7)	9.7 (6.1-13.4)	2.10 (1.19-3.68)[e]	18.5 (11.2-25.8)	1.85 (1.14-2.96)[e]	16.6 (10.6-22.6)	1.91 (1.03-3.54)[e]	17.1 (10.2-24.1)
≥2 h/d	363/1592	20.1 (1.8)	10.6 (7.1-14.0)	2.28 (1.45-3.59)[f]	21.3 (15.4-27.2)	2.21 (1.48-3.32)[d]	20.8 (15.5-26.0)	3.02 (1.77-5.14)[d]	26.3 (19.2-33.4)
Missing	114/487	20.4 (2.6)	12.8 (6.9-18.8)	1.84 (0.79-4.29)	21.3 (10.5-32.2)	2.18 (0.95-5.00)	24.3 (13.0-35.5)	2.21 (1.04-4.73)[e]	24.5 (12.2-36.9)
Caloric intake vs active child of same age and sex[h]									
>USDA cut point	133/798	14.7 (1.5)	7.6 (3.6-11.6)	2.34 (1.13-4.82)[e]	16.2 (9.3-23.1)	2.29 (1.14-4.59)[e]	15.9 (11.1-20.7)	3.24 (1.28-8.19)[e]	21.1 (10.6-31.5)
≤USDA cut point	457/2018	19.0 (1.5)	10.9 (8.0-13.9)	2.22 (1.49-3.30)[d]	21.5 (16.0-26.9)	2.05 (1.37-3.06)[f]	20.2 (15.0-25.3)	2.35 (1.56-3.54)[d]	22.4 (17.0-27.8)
Missing	29/134	14.9 (3.4)	7.4 (–0.06 to 14.9)	3.50 (0.84-14.63)	21.6 (1.7-41.6)	2.87 (0.49-17.00)	18.5 (3.6-33.4)	3.07 (0.68-13.88)	19.5 (3.4-35.6)

Abbreviations: OR, odds ratio; USDA, United States Department of Agriculture.

[a] Logistic regression analysis conducted across bisphenol A quartiles of exposure (with quartile 1 as reference group), adjusted for urinary creatinine concentration. [b] Quartile 1: values <1.5 ng/mL; quartile 2: values 1.5-2,7 ng/mL; quartile 3: values 2.8-5.5 ng/mL; quartile 4, values ≥5.6 ng/mL. [c] Weighted using environmental subsample B weight, per National Center for Health Statistics direction. [d] $P < .001$. [e] $P < .05$. [f] $P < .01$. [g] More educated indicates some college or more. [h] USDA cut point indicates cut point for children with high physical activity.

Table 3. Association of Urinary Bisphenol A Concentration and Body Mass Outcomes From Full Multivariable Models[a]

	Body Mass Outcome				
		Overweight		Obesity	
	Increment in BMI *z* Score (95% CI)	OR (95% CI)	Prevalence (95% CI), %	OR (95% CI)	Prevalence (95% CI), %
Urinary bisphenol A concentration quartile					
1	1 [Reference]	1 [Reference]	31.1 (25.4 to 36.8)	1 [Reference]	10.3 (7.5 to 13.1)
2	0.12 (–0.02 to 0.27)	1.26 (0.96 to 1.64)	36.0 (30.8 to 41.2)	2.24 (1.54 to 3.24)[b]	20.1 (14.5 to 25.6)
3	0.16 (0.01 to 0.30)[c]	1.28 (0.98 to 1.66)	36.4 (29.9 to 42.8)	2.08 (1.46 to 2.96)[b]	19.0 (13.7 to 24.2)
4	0.22 (0.06 to 0.39)[d]	1.26 (0.86 to 1.82)	35.9 (29.7 to 42.2)	2.57 (1.72 to 3.83)[b]	22.3 (16.6 to 27.9)
Log-transformed bisphenol A concentration, ng/mL	0.06 (0.001 to 0.11)[c]	1.04 (0.92 to 1.18)		1.24 (1.08 to 1.44)[d]	

[a] For all models, n = 2814. All models control for sex, caloric intake, television watching, poverty to income ratio, parental education, serum cotinine level, urinary creatinine level, age, and race/ethnicity categories.
[b] $P < .001$.
[c] $P < .05$.
[d] $P < .01$.

interaction with race/ethnicity (eTable 1, available at http://www.jama.com).

In linear and logistic regressions of body mass outcomes against log-transformed urinary BPA concentrations (eTable 1), an interaction between white race and log-transformed BPA concentration was confirmed when obesity was the outcome (OR, 1.34 [95% CI, 1.05-1.72]; $P = .02$) but not when BMI *z* score was the outcome ($P \geq .38$ for interaction terms).

Although the association was stronger in male participants, interaction terms were not significant, suggesting absence of an interaction between sex and urinary BPA concentration ($P \geq .30$ for all 3 quartiles). When log-transformed urinary BPA concentrations were substituted for quartiled concentrations, a significant interaction between sex and urinary BPA concentration was not found ($P = .23$). There was little other evidence of heterogeneity of association in subgroups.

Table 3 presents results of full multivariable linear and logistic regression analyses of body mass outcomes and their association with quartiles of urinary BPA concentrations in the entire sample. Compared with the first quartile (estimated prevalence of obesity, 10.3% [95% CI, 7.5%-13.1%]; estimated mean BMI *z* score, 0.38 [95% CI, 0.26-0.50]), the third quartile was associated with a 0.16-SD (95% CI, 0.01-0.30; $P = .04$) increment in BMI *z* score, an OR of 2.08 for obesity (95% CI, 1.46-2.96; $P < .001$), and a 19.0% estimated prevalence of obesity (95% CI, 13.7%-24.2%). The highest quartile was associated with a 0.22-SD (95% CI, 0.06-0.39, $P = .008$) increment in BMI *z* score, an OR of 2.57 for obesity (95% CI, 1.72-3.83; $P < .001$), and a 22.3% estimated prevalence of obesity (95% CI, 16.6%-27.9%). Corresponding ORs and increments in BMI *z* score are provided for all covariates in the full multivariable model, including stratified analysis, in eTables 2 and 3. We note that excessive caloric intake was inversely associated with elevations in body mass, which could reflect underreporting bias or behavioral changes by those children and their families to reduce body mass.

Specificity of Association

In bivariate analysis, urinary metabolites of other phenols were not associated with overweight or obesity (eTable 4), with the exception of urinary benzophenone level with obesity. However, that association was nonmonotonic and likely arose by chance. When added to final multivariable models with urinary BPA concentration quartiles, the other environmental phenols were not associated with obesity, nor did they significantly perturb associations of BPA concentration with obesity or BMI *z* score (eTable 5A and B). Inclusion of NHANES wave covariates to account for differences in method used to measure creatinine levels attenuated the association of third-quartile BPA concentration with BMI *z* score to $P = .055$ but did not affect other associations (eTable 6). In a complete case analysis (excluding all cases with missing covariates, n = 1858), only association of the third-quartile BPA concentration with BMI *z* score attenuated to nonsignificance. Relationships of log-transformed BPA concentration with BMI *z* score and categorical obesity remained significant (eTable 7).

COMMENT

To our knowledge, this is the first report of an association of an environmental chemical exposure with childhood obesity in a nationally representative sample. The association was evident when exposure and outcome were modeled in a number of different ways. For example, compared with the lowest quartile of urinary BPA concentration, values in the second, third, and fourth quartiles showed a substantial elevation in the odds of obesity, controlling for an array of potential confounders. This translates into an adjusted prevalence of obesity of 22.3% (95% CI, 16.6%-27.9%) among children in the highest quartile, compared with a 10.3% prevalence (95% CI, 7.5%-13.1%) among those in the lowest quartile.

This cross-sectional study, when considered in isolation, is at best hypothesis generating. Relative to similar published cross-sectional studies of urinary BPA in adults,[11,13] we included comparatively rich information about demographics, exposures, and lifestyle variables, thus providing more convincing evidence for nonspuriousness of the association. Our results are similar to associations of BPA concentration with obesity in adults identified using NHANES 2003-2006.[11] The absence of an association between body mass/obesity and levels of other environmental phenols argues for a specificity of association.

Obesity develops over time, and causation cannot be inferred from a cross-sectional association of urinary BPA concentration with increased body mass, even when consistent with increasing laboratory evidence.[28,29] Endocrine-disrupting chemicals such as BPA may have their greatest effect in early life[30] rather than in the period from ages 6 through 19 years examined in this study.

The relationship between BPA exposure and urinary BPA concentration is complex. In population studies, it is difficult to definitively document the relationship between BPA exposure and excretion in a way that would be possible in the laboratory. To date, there have been no pharmacokinetic studies in children. If BPA is rapidly and completely excreted, as suggested by the few adult pharmacokinetic studies to date,[5] then a single measurement of urinary BPA concentration would be a poor proxy for long-term exposure. Recent data from adults in NHANES 2003-2004, however, suggest that urinary BPA concentration does not decrease rapidly with fasting time, suggesting that it is stored in fat or other physiologic compartments.[4]

Even if urinary BPA concentration does not solely reflect recent consumption, it is likely to be a "noisy" indicator of chronic exposure. Studies with serial measurements of urinary BPA have identified Pearson correlation coefficients in the range of 29% to 64% over 1- to 6-month periods.[26,31,32] Time of urine collection may also influence BPA concentration.[33] A recent study documenting within-person variability in urinary BPA levels nonetheless concluded that when "samples are collected from a large number of persons (e.g. population surveys like NHANES) and randomly collected relative to meal ingestion times and bladder emptying times, the single spot-sampling approach may reflect the average exposure of a population to BPA."[34] In addition, if current concentration of urinary BPA is a noisy index of early life exposure, our estimates of association should be biased toward the null.[35]

Knowledge gaps also persist in understanding how food is contaminated with BPA. Although one detailed study has suggested that dietary sources constitute 99% of BPA exposure in children[3] and multiple studies have measured BPA levels in canned foods,[1,36-38] data from a more representative and comprehensive sample of US foods are still lacking. BPA content in food perhaps reflects pH (with markedly acidic or alkaline foods likely to have lower BPA content compared with foods with a pH of 5) as much if not more than food type and packaging.[1] Racial/ethnic differences in urinary BPA concentrations and associations of urinary BPA concentration with body mass may also reflect differences in food choices.[2] Data from NHANES 2005-2006 suggest associations of consumption of soda, school lunches, and meals prepared outside the home—but not bottled water or canned tuna—with urinary BPA concentrations.[39] Insofar as food uses of polycarbonate plastics have been reduced (as reflected in the recent Food and Drug Administration [FDA] ban on BPA in sippy cups and baby bottles),[40] then examination of BPA content in US foods as currently produced is needed.

The nonmonotonic association with obesity identified here, even though it was also identified in adults,[11] could alternatively represent some unmeasured confounder in the first quartile of BPA concentration that lowers the prevalence of obesity. This concern is somewhat diminished by the linear relationship to the logarithm of urinary concentration. Perhaps more importantly, hundreds of studies to date have documented nonmonotonic dose-response relationships in humans, animals, and cell cultures across a wide array of environmental chemicals.[41] Birnbaum[42] has emphasized that nonmonotonic associations are common for endocrine disruptors, have molecular mechanistic support, and should not be dismissed, especially as a matter of informing regulatory decision making.

Is our evidence consistent with reverse causation—for example, with obese children ingesting more BPA-containing foods? Although we adjusted for caloric intake, we do not know whether the sources of calories consumed differ between obese and nonobese children. Obese children may drink more canned or bottled beverages, or eat more canned food, and thus have higher urinary BPA levels. Similarly, although we adjusted for excessive caloric intake and television watching—2 lifestyle-associated risks for childhood obesity—it may be that sedentary children consume foods high in BPA. Obese children could also have higher urinary BPA concentrations because BPA is stored and released from adipose tissue. We cannot rule out these alternative explanations in a cross-sectional design.

Our finding of the specificity of association in white participants is only confirmed in interaction tests for obesity as an outcome and not for BMI *z* score. This specificity still merits further discussion but presents difficulty in interpretation. It could suggest spuriousness, if obese whites have unique dietary behaviors that otherwise would result in differences in urinary BPA concentrations—but we have no evidence that this is so. Another interpretation is that BPA exposure interacts with the genome or epigenome to yield different effects in racial/ethnic subgroups. The sex predilection of the association identified here, while not confirmed in

models including interaction terms, is not surprising, given the known association of obesity with increased estrogen levels in males[43] and the mild estrogenic activity of BPA.[44]

To date, research has primarily centered around the role of BPA in adult disease (with the exception of child neurodevelopment).[45] Although concerns have been raised over the last decade that synthetic chemicals might act as obesogens, few data have been available from human studies. Our national, cross-sectional analysis drawing on recent data is relevant and generalizable. Longitudinal studies with detailed data on potential confounders and other potential environmental obesogens collected at earlier windows of endocrine development (when exposures are more likely to have an effect[30]) are needed.

Advocates and policy makers have long been concerned about BPA exposure. We note the recent FDA ban of BPA in baby bottles and sippy cups,[40] yet our findings raise questions about exposure to BPA in consumer products used by older children. Last year, the FDA declined to ban BPA in aluminum cans and other food packaging, announcing "reasonable steps to reduce human exposure to BPA in the human food supply" and noting that it will continue to consider evidence on the safety of the chemical.[46] Carefully conducted longitudinal studies that assess the associations identified here will yield evidence many years in the future. The National Institutes of Health and other US government agencies[47] have encouraged such long-term studies of BPA and other putative obesogens.[28]

CONCLUSIONS

In this cross-sectional study of children and adolescents, urinary BPA concentration was significantly associated with obesity. For researchers, next steps could include research conducted among children already enrolled in longitudinal studies, measuring urinary BPA concentrations in banked samples. Ultimately, the strongest evidence will come from prospective studies with meticulous longitudinal data collection.

Author Contributions: Dr Trasande had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Trasande.
Acquisition of data: Trasande.
Analysis and interpretation of data: Trasande, Attina, Blustein.
Drafting of the manuscript: Trasande, Blustein.
Critical revision of the manuscript for important intellectual content: Trasande, Attina, Blustein.
Statistical analysis: Trasande, Attina, Blustein.
Administrative, technical, or material support: Attina.
Study supervision: Trasande.
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Online-Only Material: eTables 1-7 are available at http://www.jama.com.

REFERENCES

1. Schecter A, Malik N, Haffner D, et al. Bisphenol A (BPA) in U.S. food. *Environ Sci Technol*. 2010; 44(24):9425-9430.
2. Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. *Environ Health Perspect*. 2008;116(1):39-44.
3. Wilson NK, Chuang JC, Morgan MK, Lordo RA, Sheldon LS. An observational study of the potential exposures of preschool children to pentachlorophenol, bisphenol-A, and nonylphenol at home and daycare. *Environ Res*. 2007;103(1):9-20.
4. Stahlhut RW, Welshons WV, Swan SH. Bisphenol A data in NHANES suggest longer than expected half-life, substantial nonfood exposure, or both. *Environ Health Perspect*. 2009;117(5):784-789.
5. Völkel W, Colnot T, Csanády GA, Filser JG, Dekant W. Metabolism and kinetics of bisphenol A in humans at low doses following oral administration. *Chem Res Toxicol*. 2002;15(10):1281-1287.
6. Fernandez MF, Arrebola JP, Taoufiki J, et al. Bisphenol-A and chlorinated derivatives in adipose tissue of women. *Reprod Toxicol*. 2007;24(2):259-264.
7. Masuno H, Kidani T, Sekiya K, et al. Bisphenol A in combination with insulin can accelerate the conversion of 3T3-L1 fibroblasts to adipocytes. *J Lipid Res*. 2002;43(5):676-684.
8. Sakurai K, Kawazuma M, Adachi T, et al. Bisphenol A affects glucose transport in mouse 3T3-F442A adipocytes. *Br J Pharmacol*. 2004;141(2):209-214.
9. Hugo ER, Brandebourg TD, Woo JG, Loftus J, Alexander JW, Ben-Jonathan N. Bisphenol A at environmentally relevant doses inhibits adiponectin release from human adipose tissue explants and adipocytes. *Environ Health Perspect*. 2008;116 (12):1642-1647.
10. Vom Saal FS, Nagel SC, Coe BL, Angle BM, Taylor JA. The estrogenic endocrine disrupting chemical bisphenol A (BPA) and obesity. *Mol Cell Endocrinol*. 2012;354(1-2):74-84.
11. Carwile JL, Michels KB. Urinary bisphenol A and obesity: NHANES 2003-2006. *Environ Res*. 2011; 111(6):825-830.
12. Lang IA, Galloway TS, Scarlett A, et al. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. *JAMA*. 2008;300(11):1303-1310.
13. Melzer D, Rice NE, Lewis C, Henley WE, Galloway TS. Association of urinary bisphenol A concentration with heart disease: evidence from NHANES 2003/06. *PLoS One*. 2010;5(1):e8673.
14. Melzer D, Osborne NJ, Henley WE, et al. Urinary bisphenol A concentration and risk of future coronary artery disease in apparently healthy men and women. *Circulation*. 2012;125(12):1482-1490.
15. Bearer CF. How are children different from adults? *Environ Health Perspect*. 1995;103(suppl 6):7-12.
16. Trasande L, Cronk C, Durkin M, et al. Environment and obesity in the National Children's Study. *Environ Health Perspect*. 2009;117(2):159-166.
17. NHANES 2003-2004: Environmental Phenols (L24EPH_C). Centers for Disease Control and Prevention website. http://www.cdc.gov/nchs/nhanes/nhanes2003-2004/L24EPH_C.htm. Accessed August 20, 2012.
18. Lohman T, Roche A, Martore R. *Anthropometric Standardization Reference Manual*. Champaign, Ill: Human Kinetics Books; 1998.
19. Ogden CL, Kuczmarski RJ, Flegal KM, et al. Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. *Pediatrics*. 2002;109(1):45-60.
20. Measuring Guides for the Dietary Recall Interview. Centers for Disease Control and Prevention website. http://www.cdc.gov/nchs/nhanes/measuring_guides_dri/measuringguides.htm. Accessed March 27, 2012.
21. US Department of Agriculture. Dietary Guidelines for Americans. US Dept of Health and Human Services website. http://health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf. 2010. Accessed March 27, 2012.
22. Mendoza JA, Zimmerman FJ, Christakis DA. Television viewing, computer use, obesity, and adiposity in US preschool children. *Int J Behav Nutr Phys Act*. 2007;4:44.
23. Weitzman M, Cook S, Auinger P, et al. Tobacco smoke exposure is associated with the metabolic syndrome in adolescents. *Circulation*. 2005;112(6): 862-869.
24. Wilson KM, Finkelstein JN, Blumkin AK, Best D, Klein JD. Micronutrient levels in children exposed to secondhand tobacco smoke. *Nicotine Tob Res*. 2011; 13(9):800-808.
25. Overview of NHANES Survey Design and Weights. Centers for Disease Control and Prevention website. http://www.cdc.gov/nchs/tutorials/dietary/SurveyOrientation/SurveyDesign/intro.htm. 2012. Accessed April 4, 2012.
26. Teitelbaum SL, Britton JA, Calafat AM, et al. Temporal variability in urinary concentrations of phthalate metabolites, phytoestrogens and phenols among minority children in the United States. *Environ Res*. 2008;106(2):257-269.
27. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. *JAMA*. 2012; 307(5):491-497.
28. Elobeid MA, Allison DB. Putative environmental-endocrine disruptors and obesity: a review. *Curr Opin Endocrinol Diabetes Obes*. 2008;15(5):403-408.
29. Grün F, Blumberg B. Minireview: the case for obesogens. *Mol Endocrinol*. 2009;23(8):1127-1134.
30. Janesick A, Blumberg B. Endocrine disrupting chemicals and the developmental programming of adipogenesis and obesity. *Birth Defects Res C Embryo Today*. 2011;93(1):34-50.
31. Mahalingaiah S, Meeker JD, Pearson KR, et al. Temporal variability and predictors of urinary bisphenol A concentrations in men and women. *Environ Health Perspect*. 2008;116(2):173-178.
32. Nepomnaschy PA, Baird DD, Weinberg CR, Hoppin

JA, Longnecker MP, Wilcox AJ. Within-person variability in urinary bisphenol A concentrations: measurements from specimens after long-term frozen storage. *Environ Res*. 2009;109(6):734-737.
33. Braun JM, Kalkbrenner AE, Calafat AM, et al. Variability and predictors of urinary bisphenol A concentrations during pregnancy. *Environ Health Perspect*. 2011;119(1):131-137.
34. Ye X, Pierik FH, Hauser R, et al. Urinary metabolite concentrations of organophosphorous pesticides, bisphenol A, and phthalates among pregnant women in Rotterdam, the Netherlands: the Generation R study. *Environ Res*. 2008;108(2):260-267.
35. Fleiss JL, Shrout PE. The effects of measurement errors on some multivariate procedures. *Am J Public Health*. 1977;67(12):1188-1191.
36. Chapin RE, Adams J, Boekelheide K, et al. NTP-CERHR expert panel report on the reproductive and developmental toxicity of bisphenol A. *Birth Defects Res B Dev Reprod Toxicol*. 2008;83(3):157-395.
37. Lim DS, Kwack SJ, Kim KB, Kim HS, Lee BM. Risk assessment of bisphenol A migrated from canned foods in Korea. *J Toxicol Environ Health A*. 2009;72(21-22):1327-1335.
38. Thomson BM, Grounds PR. Bisphenol A in canned foods in New Zealand: an exposure assessment. *Food Addit Contam*. 2005;22(1):65-72.
39. Lakind JS, Naiman DQ. Daily intake of bisphenol A and potential sources of exposure: 2005-2006 National Health and Nutrition Examination Survey. *J Expo Sci Environ Epidemiol*. 2011;21(3):272-279.
40. Tavernise S. FDA makes it official: BPA can't be used in baby bottles and cups. *New York Times*. July 17, 2012. http://www.nytimes.com/2012/07/18/science/fda-bans-bpa-from-baby-bottles-and-sippy-cups.html. Accessed July 18, 2012.
41. Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. *Endocr Rev*. 2012;33(3):378-455.
42. Birnbaum LS. Environmental chemicals: evaluating low-dose effects. *Environ Health Perspect*. 2012;120(4):A143-A144.
43. Mauvais-Jarvis F. Estrogen and androgen receptors: regulators of fuel homeostasis and emerging targets for diabetes and obesity. *Trends Endocrinol Metab*. 2011;22(1):24-33.
44. Howdeshell KL, Hotchkiss AK, Thayer KA, Vandenbergh JG, vom Saal FS. Exposure to bisphenol A advances puberty. *Nature*. 1999;401(6755):763-764.
45. Braun JM, Kalkbrenner AE, Calafat AM, et al. Impact of early-life bisphenol A exposure on behavior and executive function in children. *Pediatrics*. 2011;128(5):873-882.
46. Update on Bisphenol A for Use in Food Contact Applications. US Food and Drug Administration website. http://www.fda.gov/newsevents/publichealthfocus/ucm064437.htm. January 2012. Accessed March 26, 2012.
47. White House Task Force on Childhood Obesity. Solving the Problem of Childhood Obesity Within a Generation. Let's Move website. http://www.letsmove.gov/sites/letsmove.gov/files/TaskForce_on_Childhood_Obesity_May2010_FullReport.pdf. May 2010. Accessed August 11, 2010.

Responsibility, not to a superior, but to one's conscience, the awareness of a duty not exacted by compulsion, the necessity to decide which of the things one values are to be sacrificed to others, and to bear the consequences of one's own decisions, are the very essence of any morals which deserve the name.

—F. A. Hayek (1899-1992)