Urinary Bisphenol A (BPA) Concentration Associates with Obesity and Insulin Resistance

Tiange Wang,* Mian Li,* Bing Chen, Min Xu, Yu Xu, Yun Huang, Jieli Lu, Yuhong Chen, Weiqing Wang, Xiaoying Li, Yu Liu, Yufang Bi, Shenghan Lai, and Guang Ning

Key Laboratory for Endocrine and Metabolic Diseases of Ministry of Health (T.W., M.L., M.X., Y.X., Y.H., J.L., Y.C., W.W., X.L., Y.L., Y.B., S.L., G.N.); Shanghai Clinical Center for Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Department of Endocrinology and Metabolism (T.W., M.L., M.X., Y.X., Y.H., J.L., Y.C., W.W., X.L., Y.L., Y.B., G.N.); and Department of Pharmacy (B.C.), Rui-Jin Hospital, Shanghai Jiao Tong University School of Medicine, E-Institute of Shanghai Universities, Shanghai 200025, China; and Department of Pathology (S.L.), Johns Hopkins University School of Medicine, Baltimore, Maryland 21205

Context: Bisphenol A (BPA) is one of the world's highest-volume chemicals in use today. Previous studies have suggested BPA disturbs body weight regulation and promotes obesity and insulin resistance. But epidemiological data in humans were limited.

Objective: Our objective was to determine whether BPA associates with obesity and insulin resistance.

Design, Setting, and Participants: This cross-sectional study included 3390 adults aged 40 yr or older, in Songnan Community, Baoshan District, Shanghai, China.

Main Outcome Measures: Questionnaire, clinical and biochemical measurements, and urinary BPA concentration were determined. Generalized overweight was defined as body mass index (BMI) of 24 to less than 28 kg/m^2 and obesity was defined as BMI of 28 kg/m^2 or higher. Abdominal obesity was defined as waist circumference at least 90 cm for men and at least 85 cm for women. Insulin resistance was defined as the index of homeostasis model assessment of insulin resistance higher than 2.50.

Results: The participants in the highest quartile of BPA had the highest prevalence of generalized obesity [odds ratio (OR) = 1.50; 95% confidence interval (CI) = 1.15–1.97], abdominal obesity (OR = 1.28; 95% CI = 1.03–1.60), and insulin resistance (OR = 1.37; 95% CI = 1.06–1.77). In participants with BMI under 24 kg/m^2, compared with the lowest quartile, the highest quartile of BPA increased the prevalence of insulin resistance by 94% (OR = 1.94; 95% CI = 1.20–3.14), but this association was not observed in those with BMI of 24 kg/m^2 or higher.

Conclusions: BPA was positively associated with generalized obesity, abdominal obesity, and insulin resistance in middle-aged and elderly Chinese adults. **(*J Clin Endocrinol Metab* 97: E0000–E0000, 2012)**

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in U.S.A.

doi: 10.1210/jc.2011-1989 Received July 7, 2011. Accepted October 21, 2011.

* T.W. and M.L. contributed equally to this article.

Abbreviations: ALT, Alanine aminotransferase; BMI, body mass index; BPA, bisphenol A; CI, confidence interval; GGT, γ-glutamyltransferase; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; NHANES, National Health and Nutrition Survey; OGTT, oral glucose tolerance test; OR, odds ratio; TC, total cholesterol; TG, triglycerides.

Bisphenol A (BPA), an environmental estrogen, is one of the world's highest-volume chemicals in use today (1–3). Studies *in vivo* have shed light on the mechanisms by which BPA disturbs body weight regulation and promotes obesity, including effects of BPA on adipocyte differentiation, lipid accumulation, insulin resistance, glucose transport, and adiponectin secretion (4–7). Data from the U.S. National Health and Nutrition Survey (NHANES) 2003–2004 and 2005–2006 reported a positive association between BPA and obesity (8). Recent human data showed a positive relationship between BPA and insulin resistance in women with polycystic ovary syndrome (9). However, epidemiological study was limited, and whether BPA associates with obesity and insulin resistance was still needed to be confirmed.

In the present study, we aim to investigate whether higher BPA exposure associates with obesity and insulin resistance in Chinese adults aged 40 yr or older.

Subjects and Methods

Study design and participants

Subjects were recruited from Songnan Community, Baoshan District, Shanghai, China, as reported previously (10). In June and July 2008, 10,185 registered permanent residents aged 40 yr or older received a screening examination, and in June and August 2009, 3455 participants from the 10,185 residents were randomly selected and received a comprehensive survey. Among 3455 study participants with blood and urine samples included in this survey, 65 subjects were excluded due to failed collection of clinical examination results or of self-reported liver diseases, including hepatitis, cirrhosis, or malignancy. Thus, a total of 3390 participants were finally included in the analysis. The participants (3390 subjects) and the nonparticipants (6795 subjects) were similar in characteristics such as sex and age. All procedures used in this study were in accordance with institutional guidelines. The Committee on Human Research at Rui-Jin Hospital, Shanghai Jiao-Tong University School of Medicine, approved the study protocol, and all study participants provided written informed consent.

Data collection

Sociodemographics, medical history, and lifestyle factors were documented. Weight, height, waist circumference, and blood pressure were measured by experienced nurses. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Three sitting blood pressure measurements taken consecutively at 5-min intervals using an automated electronic device (OMRON model HEM-752 FUZZY; Omron Co., Dalian, China) were averaged for analysis. All the participants were subjected to a 75-g oral glucose tolerance test (OGTT), and blood samples were collected at 0 and 2 h during the OGTT. Plasma glucose was measured using the glucose oxidase method on an autoanalyzer (ADVIA-1650 Chemistry System; Bayer Corp., Leverkusen, Germany), and serum insulin concentration was measured by an electrochemiluminescence assay (Roche Diagnostics, Basel, Switzerland). Measurements of urinary creatinine, serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), alanine aminotransferase (ALT), γ-glutamyltransferase (GGT), and high-sensitivity C-reactive protein (hs-CRP) were performed with an autoanalyzer (ADVIA-1650 Chemistry System).

Total (free and conjugated) urinary BPA concentration was measured in a spot morning urine sample by a sensitive and selective liquid chromatography-tandem mass spectrometry at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, as reported previously (10). For BPA concentrations less than 0.30 ng/ml, the lower limit of quantification, a value of 0.15 ng/ml was assigned for the purpose of analysis (11).

Generalized overweight was defined as having a BMI of 24 to less than 28 kg/m^2, and obesity was defined as having a BMI of28 kg/m^2 or higher according to Chinese criteria (12). Abdominal obesity was defined using the Chinese criteria as waist circumference at least 90 cm for men and at least 85 cm for women (13). Insulin resistance was defined as homeostasis model assessment of insulin resistance (HOMA-IR) higher than 2.50.

Statistical analysis

Statistical analysis was performed with SAS version 8.1 (SAS Institute, Cary, NC), and a P value <0.05 (two sided) indicated statistical significance. Data were summarized as means and SD for continuous variables or numbers and percentages for categorical parameters. The concentrations of urinary BPA, serum TG, fasting insulin, hs-CRP, ALT, and GGT were logarithmically transformed to achieve a normal distribution. Linear regression analysis was used to test for trend of the changes of variables across the quartiles of urinary BPA concentrations, and logistic regression models were employed to evaluate the odds ratios (OR) and 95% confidence intervals (CI) of having generalized overweight and obesity, abdominal obesity, and insulin resistance for higher quartiles of BPA compared with the lowest quartile.

Results

Compared with the participants in the lowest quartile, those in the highest quartile of urinary BPA were younger and more likely to be men and had significantly higher BMI, waist circumference, fasting plasma glucose, fasting serum insulin, and GGT and lower HDL-C and urinary creatinine concentration (all P for trend <0.05) (Table 1).

Table 2 shows that increased BPA was associated with an increased prevalence of generalized and abdominal obesity. Compared with the first quartile, the OR (95% CI) for generalized obesity were 1.14 (0.87–1.50) for the second, 1.19 (0.90–1.57) for the third, and 1.50 (1.15–1.97) for the fourth quartile of urinary BPA concentration, after adjusting for age, sex, urinary creatinine, smoking, alcohol drinking, education levels, systolic blood pressure, HDL-C, LDL-C, TC, TG, hs-CRP, fasting plasma glucose, fasting serum insulin, ALT, and GGT. There was no significant association between increased urinary BPA and

TABLE 1. General demographic and laboratory characteristics of the 3390 study participants

		BPA quartiles (ng/ml)					
	Total	Quartile 1 (≤0.47)	Quartile 2 (0.48–0.81)	Quartile 3 (0.82–1.43)	Quartile 4 (>1.43)	Unadjusted *P* for trend	Adjusted *P* for trend[a]
Participants (n)	3390	851	848	847	844		
BPA (ng/ml)	0.81 (0.47–1.43)	0.30 (0.15–0.39)	0.63 (0.56–0.72)	1.04 (0.91–1.21)	2.28 (1.76–3.29)		
Age (yr)	60.8 ± 9.9	63.3 ± 10.2	61.5 ± 9.9	59.6 ± 9.6	58.8 ± 9.5	<0.001	
Male sex [n (%)]	1356 (40.0)	269 (31.6)	341 (40.2)	355 (41.9)	391 (46.3)	<0.001	
Educational attainment [n (%)]							
≤6 yr	760 (22.8)	253 (30.2)	191 (22.8)	163 (19.6)	153 (18.4)	<0.001	0.38
6.1–8.9 yr	1645 (49.3)	379 (45.2)	423 (50.5)	418 (50.4)	425 (51.1)		
≥9 yr	932 (27.9)	206 (24.6)	224 (26.7)	249 (30.0)	253 (30.5)		
Smoking status [n (%)]							
Never smokers	2495 (73.9)	688 (80.8)	625 (74.1)	615 (73.0)	589 (67.7)	<0.001	0.27
Ex-smokers	177 (5.2)	46 (5.4)	42 (5.0)	44 (5.2)	45 (5.4)		
Current smokers	705 (20.9)	117 (16.6)	177 (25.1)	184 (21.8)	227 (27.0)		
Alcohol consumption [n (%)]							
Never drinkers	2801 (82.9)	748 (88.1)	695 (82.4)	699 (82.9)	659 (78.4)	<0.001	0.12
Ex-drinkers	39 (1.2)	8 (0.9)	8 (0.9)	11 (1.3)	12 (1.4)		
Current drinkers	537 (15.9)	93 (11.0)	141 (16.7)	133 (15.8)	170 (20.2)		
BMI (kg/m^2)	24.9 ± 3.6	24.6 ± 3.6	24.9 ± 3.8	24.8 ± 3.6	25.1 ± 3.5	0.013	<0.001
Waist circumference (cm)	87.3 ± 9.8	86.6 ± 9.9	87.7 ± 9.8	87.1 ± 9.8	87.9 ± 9.6	0.028	<0.001
Systolic blood pressure (mm Hg)	138 ± 22	142 ± 24	140 ± 22	137 ± 21	136 ± 20	<0.001	0.10
TC (mmol/liter)	5.15 ± 0.99	5.19 ± 1.04	5.17 ± 0.98	5.14 ± 0.99	5.10 ± 0.93	0.047	0.99
LDL-C (mmol/liter)	2.39 ± 0.69	2.42 ± 0.71	2.37 ± 0.69	2.38 ± 0.70	2.39 ± 0.65	0.54	0.63
HDL-C (mmol/liter)	1.35 ± 0.31	1.39 ± 0.33	1.36 ± 0.31	1.35 ± 0.29	1.32 ± 0.29	<0.001	<0.001
TG (mmol/liter)	1.44 (0.73–2.08)	1.44 (1.01–2.05)	1.43 (0.98–2.08)	1.44 (1.00–2.11)	1.46 (1.01–2.10)	0.24	0.068
Fasting plasma glucose (mmol/liter)	5.8 ± 1.9	5.6 ± 1.6	5.9 ± 2.1	5.8 ± 2.0	5.9 ± 1.9	0.019	0.001
Fasting serum insulin (μIU/ml)	7.21 (4.71–10.80)	7.17 (4.74–10.80)	7.32 (4.69–10.86)	7.05 (4.57–10.35)	7.28 (4.76–11.11)	0.93	0.009
hs-CRP (mg/liter)	0.20 (0.06–0.85)	0.20 (0.06–0.90)	0.21 (0.07–0.89)	0.18 (0.06–0.71)	0.22 (0.07–0.83)	0.58	0.092
ALT (U/liter)	19 (13–27)	18 (13–26)	19 (13–28)	18 (13–27)	20 (14–29)	0.086	0.32
GGT (U/liter)	24 (17–36)	22 (16–33)	24 (17–37)	24 (17–36)	25 (18–39)	0.003	0.030
Urinary creatinine (μmol/liter)	77.1 ± 3.7	77.5 ± 3.7	77.1 ± 3.8	77.1 ± 3.6	76.7 ± 3.8	<0.001	

Data are means ± SD, median (interquartile range), or number (proportion) for categorical variables.

[a] *P* values were adjusted for age, sex, and urinary creatinine.

generalized overweight in the similar fully adjusted logistic regression model. Relative to the first quartile, the OR (95% CI) for abdominal obesity were 1.26 (1.02–1.57) for the second, 1.28 (1.03–1.59) for the third, and 1.28 (1.03–1.60) for the fourth quartile in the fully adjusted model.

For insulin resistance, the fourth quartile of urinary BPA had the highest OR (1.56; 95% CI = 1.26–1.94) in the age-, sex-, and urinary creatinine-adjusted model. After further adjusting for BMI, waist circumference, smoking, alcohol drinking, education levels, systolic blood pressure, HDL-C, LDL-C, TC, TG, hs-CRP, ALT, and GGT, the fourth quartile increased the prevalence of insulin resistance by 37% (OR = 1.37; 95% CI = 1.06–1.77), compared with the first quartile. In the participants with BMI under 24 kg/m^2 (n = 1401), the OR (95% CI) for insulin resistance were 1.55 (0.97–2.46) for the second, 1.04 (0.64–1.70) for the third, and 1.94 (1.20–3.14) for the fourth quartile after full adjustment. In the participants with BMI of 24 kg/m^2 or higher (n = 1989), the age-, sex-, and urinary creatinine-adjusted OR (95% CI) for insulin resistance were 1.03 (0.79–1.35), 1.09 (0.84 to1.43), and 1.26 (0.97 to1.65) for quartile 2, 3, and 4, respectively. After further adjustment, still no significant association was observed (Table 2).

Discussion

In this study among 3390 Chinese adults aged 40 yr and older, we reported a positive and significant association between urinary BPA concentration and the prevalence of generalized obesity, abdominal obesity, and insulin resistance.

Obesity is a multifactorial disease influenced by a complex interaction between genetic, behavioral, and environmental factors (14, 15). Several potential mechanisms could account for the actions of BPA in the development of obesity. First, *in vitro* studies of 3T3-L1 cells have revealed that micromolar concentration of BPA could enhance adipocyte differentiation and lipid accumulation in target cells, and BPA was found to increase gene expression of adipogenic transcription factors in 3T3-L1 preadipocytes (16). If similar effects of BPA occur *in vivo*, they would be expected to play an important role in increasing adiposity and body weight. Second, results of *in vitro* studies have indicated similarities between the action of estradiol and BPA on the inhibition of adiponectin secretion from human adipocyte in a dose-dependent manner (16). And BPA has been found to increase insulin, mimicking estradiol, and influence the insulin-secreting β-cells and glucagon-secreting α-cells of the pancreas, leading to hy-

TABLE 2. Association between urinary bisphenol A concentration and obesity, insulin resistance

	BPA quartiles (ng/ml)			
	Quartile 1 (≤0.47)	**Quartile 2 (0.48–0.81)**	**Quartile 3 (0.82–1.43)**	**Quartile 4 (>1.43)**
Generalized overweight[a]				
Cases/participants	329/707	354/698	345/702	344/666
Age-, sex-, and urinary creatinine-adjusted OR (95% CI)	1.00	1.20 (0.97–1.48)	1.15 (0.93–1.43)	1.29 (1.04–1.61)
Multivariate adjusted OR (95% CI)[b]	1.00	1.23 (0.97–1.57)	1.28 (1.01–1.63)	1.24 (0.97–1.59)
Generalized obesity				
Cases/participants	144/851	150/848	145/847	178/844
Age-, sex-, and urinary creatinine-adjusted OR (95% CI)	1.00	1.15 (0.89–1.48)	1.16 (0.89–1.50)	1.57 (1.22–2.01)
Multivariate adjusted OR (95% CI)[b]	1.00	1.14 (0.87–1.50)	1.19 (0.90–1.57)	1.50 (1.15–1.97)
Abdominal obesity				
Cases/participants	389/851	417/848	394/847	407/844
Age-, sex-, and urinary creatinine-adjusted OR (95% CI)	1.00	1.29 (1.06–1.57)	1.25 (1.03–1.53)	1.43 (1.17–1.74)
Multivariate adjusted OR (95% CI)[b]	1.00	1.26 (1.02–1.57)	1.28 (1.03–1.59)	1.28 (1.03–1.60)
Insulin resistance				
Cases/participants	248/851	268/848	250/847	282/844
Age-, sex-, and urinary creatinine-adjusted OR (95% CI)	1.00	1.27 (1.02–1.57)	1.20 (0.97–1.50)	1.56 (1.26–1.94)
Multivariate adjusted OR (95% CI)[c]	1.00	1.18 (0.92–1.52)	1.09 (0.85–1.42)	1.37 (1.06–1.77)
Insulin resistance in participants with BMI <24 kg/m^2 (n = 1401)				
Cases/participants	47/331	58/344	45/357	53/322
Age-, sex-, and urinary creatinine adjusted OR (95% CI)	1.00	1.75 (1.14–2.68)	1.31 (0.83–2.06)	2.00 (1.28–3.13)
Multivariate adjusted OR (95% CI)[c]	1.00	1.55 (0.97–2.46)	1.04 (0.64–1.70)	1.94 (1.20–3.14)
Insulin resistance in participants with BMI ≥24 kg/m^2 (n = 1989)				
Cases/participants	201/473	210/504	205/490	229/522
Age-, sex- ,and urinary creatinine-adjusted OR (95% CI)	1.00	1.03 (0.79–1.35)	1.09 (0.84–1.43)	1.26 (0.97–1.65)
Multivariate adjusted OR (95% CI)[c]	1.00	1.06 (0.78–1.43)	1.11 (0.81–1.51)	1.21 (0.89–1.64)

[a] For the risk of generalized overweight, we defined participants with a BMI less than 24 as 0 (n = 1401) and generalized overweight as 1 (n = 1372), excluding obesity participants (n = 617) from the analysis.

[b] The OR (95% CI) were adjusted for age, sex, urinary creatinine concentration, smoking, alcohol drinking, education levels, systolic blood pressure, HDL-C, LDL-C, TC, TG, hs-CRP, fasting plasma glucose, fasting serum insulin, and serum ALT and GTT.

[c] The OR (95% CI) were further adjusted for BMI based on the adjustment indicated in *footnote b*.

perinsulinemia and finally to insulin resistance, a factor contributing to the development of obesity (4, 5). Third, numerous studies have shed light on the effect of BPA on the developing of the brain, which is a sensitive target organ for BPA (17). Early exposure to BPA could disturb the development and maturation of brain circuits, which contribute to the regulation of food intake and metabolism, which start during the perinatal period, and then affect energy homeostasis (18).

Recently, the pooled data from 2003–2004 and 2005–2006 NHANES reported a positive association between BPA and obesity (8). They found that the OR for generalized and abdominal obesity were more prominent in quartile 2 of BPA than in other quartiles, whereas we found a gradual increasing of the OR according to the increment of BPA quartiles for generalized obesity and the highest OR of the fourth BPA quartile for abdominal obesity. Kandaraki *et al.* (9) found that BPA was positively associated with Matsuda index in women with polycystic ovary syndrome ($r = 0.273$; $P < 0.05$), indicating a possible impact of BPA on insulin action. We found a positive association between BPA and insulin resistance that was evaluated by HOMA-IR, and the effect of BPA was more prominent in participants with BMI less than 24 kg/m^2 than those with higher BMI. In our data, BPA concentration was higher in participants with higher BMI [0.82 (0.49–1.47) ng/ml] than those with lower BMI [0.79 (0.44–1.38) ng/ml], and the percentage of males was not significantly different in participants with higher BMI (40.8%) and with lower BMI (38.8%). Insulin resistance is closely associated with obesity (19), and the association is likely a cause-and-effect relationship because human and animal studies demonstrated that weight loss significantly correlates with increasing insulin sensitivity, whereas weight gain significantly correlates with decreasing insulin sensitivity (20). Our results suggested that the association between BPA and insulin resistance may be modulated by BMI, because the relationship between BMI and HOMA-IR was more prominent ($\beta = 1.51$; $P < 0.0001$) in participants with higher BMI than in those with less BMI ($\beta = 0.79$; $P < 0.0001$), the effect of higher BMI may overwhelm that of BPA on insulin resistance in participants with higher BMI.

Our study has several limitations. First, due to the cross-sectional nature, no causal relationships can be es-

tablished in the pathophysiological mechanism linking BPA with obesity and insulin resistance. Second, the analyses are based on morning urinary BPA concentrations, which reflect only recent exposure. Third, we did not collect data on dietary behaviors. BPA could be a marker of sugar beverages in plastic bottles, and intake of sugar beverages has been shown to be associated with obesity. In the absence of reliable dietary measures, any observational study that detects an association could have bias.

In conclusion, we reported that urinary BPA was positively and significantly associated with obesity and insulin resistance in Chinese adults aged 40 yr and older. The association between BPA exposure and the increased risk of obesity and insulin resistance seen in this population should be assessed in additional follow-up studies.

Acknowledgments

We thank the field workers for their contribution and the participants for their cooperation.

Address all correspondence and requests for reprints to: Yufang Bi, M.D., Shanghai Clinical Center for Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Department of Endocrine and Metabolic Diseases, Rui-Jin Hospital, Shanghai Jiao-Tong University School of Medicine, 197 Rui-Jin 2nd Road, Shanghai 200025, China. E-mail: byf10784@rjh.com.cn.

This work was supported by grants from the Key Laboratory for Endocrine and Metabolic Diseases of Ministry of Health (1994DP131044), the Sector Funds of Ministry of Health (201002002), the National Key New Drug Creation and Manufacturing Program of Ministry of Science and Technology (2008ZX09312/019), the Creative Research Group of Ministry of Education (IRT0932), the National Natural Science Foundation (30725037), the Major Project of Shanghai Committee of Science and Technology (09DZ1950200), and the National Key Technologies Research and Development Program of Ministry of Science and Technology (2008BAI52B03).

Disclosure Summary: The authors have nothing to declare.

References

1. **Burridge E** 2003 Bisphenol A: product profile. Eur Chem News 17:14–20
2. **Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL** 2008 Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003–2004. Environ Health Perspect 116:39–44
3. **Dekant W, Völkel W** 2008 Human exposure to bisphenol A by biomonitoring: methods, results and assessment of environmental exposures. Toxicol Appl Pharmacol 228:114–134
4. **Ropero AB, Alonso-Magdalena P, García-García E, Ripoll C, Fuentes E, Nadal A** 2008 Bisphenol-A disruption of the endocrine pancreas and blood glucose homeostasis. Int J Androl 31:194–200
5. **Alonso-Magdalena P, Morimoto S, Ripoll C, Fuentes E, Nadal A** 2006 The estrogenic effect of bisphenol A disrupts pancreatic β-cell function *in vivo* and induces insulin resistance. Environ Health Perspect 114:106–112
6. **Masuno H, Iwanami J, Kidani T, Sakayama K, Honda K** 2005 Bisphenol A accelerates terminal differentiation of 3T3-L1 cells into adipocytes through the phosphatidylinositol 3-kinase pathway. Toxicol Sci 84:319–327
7. **Hugo ER, Brandebourg TD, Woo JG, Loftus J, Alexander JW, Ben-Jonathan N** 2008 Bisphenol A at environmentally relevant doses inhibits adiponectin release from human adipose tissue explants and adipocytes. Environ Health Perspect 116:1642–1647
8. **Carwile JL, Michels KB** 2011 Urinary bisphenol A and obesity: NHANES 2003–2006. Environ Res 111:825–830
9. **Kandaraki E, Chatzigeorgiou A, Livadas S, Palioura E, Economou F, Koutsilieris M, Palimeri S, Panidis D, Diamanti-Kandarakis E** 2011 Endocrine disruptors and polycystic ovary syndrome (PCOS): elevated serum levels of bisphenol A in women with PCOS. J Clin Endocrinol Metab 96:E480–E484
10. **Ning G, Bi Y, Wang T, Xu M, Xu Y, Huang Y, Li M, Li X, Wang W, Chen Y, Wu Y, Hou J, Song A, Liu Y, Lai S** 2011 Relationship of urinary bisphenol A concentration to risk for prevalent type 2 diabetes in Chinese adults. Ann Intern Med 155:368–374
11. **He Y, Miao M, Herrinton LJ, Wu C, Yuan W, Zhou Z, Li DK** 2009 Bisphenol A levels in blood and urine in a Chinese population and the personal factors affecting the levels. Environ Res 109:629–633
12. **Zhou BF** 2002 Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults: study on optimal cut-off points of body mass index and waist circumference in Chinese adults. Biomed Environ Sci Mar 15:83–96
13. **Bao Y, Lu J, Wang C, Yang M, Li H, Zhang X, Zhu J, Lu H, Jia W, Xiang K** 2008 Optimal waist circumference cutoffs for abdominal obesity in Chinese. Atherosclerosis 201:378–384
14. **Hu FB** 2008 Obesity epidemiology. New York: Oxford University Press
15. **Ogden CL, Yanovski SZ, Carroll MD, Flegal KM** 2007 The epidemiology of obesity. Gastroenterology 132:2087–2102
16. **Masuno H, Kidani T, Sekiya K, Sakayama K, Shiosaka T, Yamamoto H, Honda K** 2002 Bisphenol A in combination with insulin can accelerate the conversion of 3T3-L1 fibroblasts to adipocytes. J Lipid Res 43:676–684
17. **Rubin BS, Lenkowski JR, Schaeberle CM, Vandenberg LN, Ronsheim PM, Soto AM** 2006 Evidence of altered brain sexual differentiation in mice exposed perinatally to low environmentally relevant levels of bisphenol A. Endocrinology 147:3681–3691
18. **Xiao XQ, Williams SM, Grayson BE, Glavas MM, Cowley MA, Smith MS, Grove KL** 2007 Excess weight gain during the early postnatal period is associated with permanent reprogramming of brown adipose tissue adaptive thermogenesis. Endocrinology 148:4150–4159
19. **Saltiel AR, Kahn CR** 2001 Insulin signaling and the regulation of glucose and lipid metabolism. Nature 414:799–806
20. **Freidenberg GR, Reichart D, Olefsky JM, Henry RR** 1988 Reversibility of defective adipocyte insulin receptor kinase activity in non-insulin-dependent diabetes mellitus. Effect of weight loss. J Clin Invest 82:1398–1406