Iodine Status and Thyroid Function of Boston-Area Vegetarians and Vegans

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Context: Adequate dietary iodine is required for normal thyroid function. The iodine status and thyroid function of U.S. vegetarians and vegans have not been previously studied. Environmental perchlorate and thiocyanate (inhibitors of thyroid iodine uptake) exposures may adversely affect thyroid function.

Objective: The objective of the study was to assess the iodine status and thyroid function of U.S. vegetarians (consume plant based products, eggs, milk; abstain from meat, poultry, fish, shellfish) and vegans (avoid all animal products) and whether these may be affected by environmental perchlorate and thiocyanate exposures.

Design and Setting: This was a cross-sectional assessment of urinary iodine, perchlorate, and thiocyanate concentrations and serum thyroid function in Boston-area vegetarians and vegans.

Subjects: One hundred forty-one subjects (78 vegetarians, 63 vegans) were recruited; one vegan was excluded.

Results: Median urinary iodine concentration of vegans (78.5 μg/liter; range 6.8–964.7 μg/liter) was lower than vegetarians (147.0 μg/liter; range 9.3–778.6 μg/liter) ($P < 0.01$). Adjusted for cigarette smoking (confirmed by urinary cotinine levels) and thiocyanate-rich food consumption, median urinary thiocyanate concentration of vegans (630 μg/liter; range 108-3085 μg/liter) was higher than vegetarians (341 μg/liter; range 31–1963 μg/liter) ($P < 0.01$). There were no between-group differences in urinary perchlorate concentrations ($P = 0.75$), TSH ($P = 0.46$), and free T_4 ($P = 0.77$). Urinary iodine, perchlorate, and thiocyanate levels were not associated with TSH ($P = 0.59$) or free T_4 ($P = 0.14$), even when adjusted for multiple variables.

Conclusions: U.S. vegetarians are iodine sufficient. U.S. vegans may be at risk for low iodine intake, and vegan women of child-bearing age should supplement with 150 μg iodine daily. Environmental perchlorate and thiocyanate exposures are not associated with thyroid dysfunction in these groups. **(*J Clin Endocrinol Metab* 96: E1303–E1307, 2011)**

Adequate iodine intake is important for thyroid hormone synthesis. Although the United States has been generally iodine sufficient since the 1920s, some individuals may be at risk for iodine deficiency. Population iodine sufficiency is defined by median urinary iodine concentrations 100 μg/liter or greater in adults and 150 μg/liter or greater in pregnancy (1). According to National Health and Nutrition Examination Surveys (NHANES), U.S. adult median urinary iodine concentrations decreased by greater than 50% from 1971 to 1994 (320 to 145 μg/liter) but in 2007–2008 remained adequate at 164 μg/liter (2).

Pregnant and lactating women are especially susceptible to iodine deficiency because the fetus and breast-fed

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Abbreviations: FT4, Free T_4; NHANES, National Health and Nutrition Examination Surveys.

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infant rely on maternal iodine intake for thyroid hormone synthesis required for normal neurodevelopment (International Council for the Control of Iodine Deficiency Disorders, http://www.iccidd.org). Between 1971 and 2008, urinary iodine levels less than 50 μg/liter among U.S. women of child-bearing age rose from 4 to 15% (2). Despite ongoing public health efforts, iodine deficiency affects more than 2.2 billion individuals and remains the leading cause of preventable mental retardation worldwide (1).

U.S. dietary iodine sources vary widely. Foods with high iodine content include iodized salt, dairy products, eggs, seafood, and some breads. However, iodine content is rarely listed on packaging, and salt iodization has never been mandated. Recent dietary salt restrictions have been associated with iodine deficiency in women (3). Vegetarians (consume plant based products, eggs, milk; abstain from meat, poultry, fish, shellfish) and vegans (avoid all animal products), comprising about 2.5% of the U.S. population, may be vulnerable to low iodine intake.

There are limited data on the iodine status of U.S. vegetarians and vegans, including two reports of neonatal hypothyroidism in vegan mothers (4, 5). Most data are from small European studies. Iodine content of a Swedish vegan diet (39 μg iodine per 1000 kcal) was lower than a mixed diet (156 μg iodine per 1000 kcal) (6), similar to the low-iodine content of German vegan diets (7). The iodine content of weighed vegan diets, which can differ widely from food records (8), among 38 British individuals was below recommended iodine intake levels (9). Urinary iodine levels were lower in Slovakian vegans (78 μg/liter) than vegetarians (172 μg/liter) (10) and far lower in 30 British vegans (20 μg/liter) (11). Studies of thyroid function in vegetarians and vegans are limited. Although serum TSH was generally normal in 101 British vegans, the geometric mean was 47% higher than for omnivores (12). No thyroid function abnormalities were found in six Swedish and 12 Finnish vegans (6, 13).

The consumption of soy, which contains the isoflavones genenstein and daidzein, may be associated with iodine deficiency and hypothyroidism. Isoflavones inhibit thyroid peroxidase activity in rats. In a review of 14 trials, isoflavone ingestion in euthyroid adults did not affect thyroid function (14). Goiters in infants fed non-iodine-fortified soy formula were reversed by changing to cows' milk or iodine-supplemented diets (15).

Iodine use may be influenced by other factors. Perchlorate, a ubiquitous environmental contaminant, is a competitive inhibitor of the sodium/iodine symporter in the thyroid and lactating breast. In high concentrations, perchlorate decreases active transport of thyroidal iodine and may decrease breast milk iodine. Perchlorate has been detected in U.S. drinking water, including Massachusetts, and in multiple foods. Perchlorate was detectable in all 2820 spot urines from NHANES 2001–2002 (median 3.6 μg/liter) (16). There has been recent concern that low-level perchlorate exposure might induce or aggravate hypothyroidism. Perchlorate exposure among vegetarians and vegans, whose iodine intake may be low, may place them at even greater risk for iodine deficiency (17).

Cigarette smoke contains thiocyanate, a less effective competitive sodium/iodine symporter inhibitor than perchlorate. Low levels of thiocyanate are found in *Brassica* genus vegetables. Individuals consuming significant amounts of these plants may be vulnerable to iodine deficiency, goiter, and hypothyroidism.

We cross-sectionally examined urinary iodine concentrations and thyroid function of Boston-area vegetarians and vegans and determined whether these may be associated with environmental perchlorate and thiocyanate exposures.

Subjects and Methods

We recruited 141 healthy Boston-area vegetarians (n = 78) and vegans (n = 63) in 2010. The Boston University Medical Campus Institutional Review Board approved the protocol. Informed consent was obtained. Subjects were 18 yr old or older and vegetarians or vegans for 3 months or longer. Exclusion criteria were thyroid disease, thyroid hormone use, pregnancy, or recent exposure to iodine-containing medications and contrast agents.

Subjects' ethnicity, birth place, age, gender, marital status, duration and strictness of diet, medical history, family history of thyroid disease, cigarette smoking, iodine-containing multivitamin or supplement use, and consumption of common iodine-containing and thiocyanate-containing foods were obtained. Subjects completed a soy food frequency questionnaire to estimate isoflavone consumption within the past month (18). Urinary spot iodine was measured spectrophotometrically. Urine perchlorate and thiocyanate concentrations were measured by ion chromatography-mass spectrometry. Urinary cotinine, a cigarette smoke specific metabolite, was measured by immunoassay (Immulite 2000; Diagnostic Products Corp., Los Angeles, CA). Serum TSH (normal 0.5–5.5 mIU/liter) and free T_4 (FT4) (normal 0.8–2.0 ng/dl) were measured by ELISA (Immuno-Biological Laboratories, Inc., Minneapolis, MN).

Statistical analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC). Descriptive characteristics are reported as mean ± SD or median (range). The Wilcoxon rank sum test assessed for between-group differences in median urinary iodine, perchlorate, and thiocyanate levels. Student's *t* test was used to compare thyroid function between vegetarians and vegans. The nonnormally distributed serum TSH values were logarithmically transformed for multivariate analyses. Pearson's or Spearman's rank correlation coefficients, as appropriate, were used to determine univariate associations. Multivariable linear regression models were used to determine significant predictors of urinary iodine levels and thyroidal function and adjusted for important covariates, confounders, and effect modifiers. The re-

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gression model for perchlorate was adjusted for thiocyanate and for the thiocyanate model, for perchlorate.

Results

One kelp-consuming vegan (urinary iodine concentration 9437 μg/liter) was excluded from all analyses. Descriptive characteristics of 140 subjects, predominantly Caucasian nonsmoking women, and vegetarian or vegan for 6–11 yr, are shown in Table 1. Most subjects had not used iodized salt in the previous 24 h and did not regularly take an iodine-containing multivitamin. Kelp use was reported in one additional vegan and one vegetarian (urinary iodine concentrations 776 and 147 μg/liter, respectively).

Median urinary iodine concentration of vegans (78.5 μg/liter; range 6.8–964.7 μg/liter) was significantly lower than vegetarians (147.0 μg/liter; range 9.3–778.6 μg/liter) ($P < 0.01$) (Table 2). There was no significant difference in urinary iodine concentrations between men and women ($P = 0.21$). Median serum TSH and FT4 concentrations were similar in both groups and in the normal range. Only one subject had a TSH above 5.5 mIU/liter (6.81 mIU/liter, in the vegan group). There was no difference in urinary perchlorate concentrations. Urinary thiocyanate concentrations were higher in vegans (630 μg/liter; range 108-3085 μg/liter) than vegetarians (341μg/liter; range 31–1963μg/liter) ($P < 0.01$). Median urinary cotinine levels were 0.22 ng/ml (range 0–2849 ng/ml) in vegetarians and 0.10 ng/ml (0–83947 ng/ml) in vegans ($P = 0.34$). There were six subjects with cotinine concentrations greater than 500 ng/ml (denoting active recent cigarette smoking) in each group. Exclusion of these individuals did not change the comparisons of median urinary iodine, perchlorate, thiocyanate, and serum thyroid function concentrations (Table 3).

Higher urinary iodine concentrations were associated with recent ingestion of cow's milk ($P = 0.03$), soy milk ($P = 0.05$), and bread ($P = 0.04$) but not cheese ($P = 0.12$), yogurt ($P = 0.15$), ice cream ($P = 0.86$), soy sauce ($P = 0.25$), eggs ($P = 0.21$), bagels ($P = 0.15$), or fish ($P = 0.25$). There were no correlations between urinary iodine, perchlorate, or thiocyanate concentrations and thyroid function, including when stratified by diet. There were no correlations between self-reported isoflavone consumption and urinary iodine ($P = 0.61$, r = −0.04), log-transformed TSH ($P = 0.26$, r = −0.10), or FT4 ($P = 0.73$, r = 0.03) levels. In multivariable regression analyses, urinary iodine, perchlorate, and thiocyanate levels were not associated with TSH ($P = 0.59$) or FT4 ($P = 0.14$), including after adjustment for age, gender, birth place, diet type, diet compliance, salt type use, cotinine levels, or isoflavone consumption ($P = 0.89$ for TSH; $P = 0.67$ for FT4).

TABLE 1. Subject characteristics

	Vegetarians (n = 78)	Vegans (n = 62)
Age (yr)	30.8 ± 10.6	36.6 ± 13.2
Race		
Caucasian	42 (54%)	51 (82%)
Black	4 (5%)	8 (13%)
Hispanic	6 (8%)	2 (3%)
Asian	22 (28%)	0 (0%)
Other	4 (5%)	1 (2%)
Country of birth		
United States	54 (69%)	57 (92%)
Other	24 (31%)	5 (8%)
Gender		
Male	26 (33%)	19 (31%)
Female	52 (67%)	43 (69%)
Marital status		
Single, never married	50 (64%)	34 (55%)
Married	18 (23%)	17 (27%)
Divorced	7 (9%)	5 (8%)
Widowed	0 (0%)	4 (6%)
Other	3 (4%)	2 (3%)
Highest level of education		
High school	13 (17%)	19 (31%)
Four-year college	36 (46%)	25 (40%)
Graduate school/professional	27 (35%)	17 (27%)
Other	2 (3%)	1 (2%)
Duration of present diet (yr)	11.3 ± 11.7	5.6 ± 5.7
Strictness of diet		
100% of the time	65 (83%)	47 (76%)
75–100% of the time	10 (13%)	14 (23%)
50–74% of the time	2 (3%)	0 (0%)
25–49% of the time	0 (0%)	1 (2%)
Less than 25% of the time	1 (1%)	0 (0%)
Use of iodized salt in last 24 h		
Yes	16 (21%)	3 (5%)
No	50 (64%)	49 (79%)
Did not know	12 (15%)	10 (16%)
Listed iodine content in daily multivitamin (μg)		
No multivitamin use	43 (55%)	31 (50%)
0	17 (22%)	7 (11%)
25	0 (0%)	2 (3%)
50	0 (0%)	1 (2%)
75	1 (1%)	3 (5%)
100	0 (0%)	2 (3%)
150	15 (19%)	14 (23%)
160	0 (0%)	1 (2%)
225	0 (0%)	1 (2%)
Regular use of kelp or other iodine supplements		
Yes	1 (1%)	2 (3%)
No	77 (99%)	60 (97%)
Self-reported cigarette smoking		
Yes	14 (18%)	5 (8%)
No	64 (82%)	57 (92%)

Number of subjects for each descriptor may not equal the total n due to missing data, and percentages may not equal 100 due to rounding.

Discussion

This is the first report of iodine nutrition and thyroid function in U.S. vegetarians and vegans. The median urinary iodine concentration of Boston-area vegans (78.5 μg/liter) was lower than in the general U.S. adult population (164 μg/liter) (2) and in the Northeast U.S. population (134

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TABLE 2. Concentrations [medians (range)] of urinary iodine, perchlorate, and thiocyanate and serum thyroid function of entire data set

	Vegetarians (n = 78)	Vegans (n = 62)	*P*
Urinary iodine (μg/liter)[a]	147.0 (9.3–778.6)	78.5 (6.8–964.7)	<0.01
Urinary perchlorate (μg/liter)[a]	4.6 (0.2–42)	3.6 (0.2–258)	0.75
Urinary thiocyanate (μg/liter)[a]	341 (31–1963)	630 (108–3085)	<0.01
Urinary cotinine (ng/ml)[a]	0.22 (0–2849)	0.10 (0–83947)	0.34
TSH (mIU/liter)[b]	1.38 (0–3.52)	1.10 (0.14–6.81)	0.46
FT4 (ng/dl)[b]	1.29 (0.95–1.66)	1.24 (0.92–1.67)	0.77

[a] n = 77 (vegetarians) and n = 62 (vegans) due to missing data.

[b] n = 76 (vegetarians) and n = 60 (vegans) due to missing data.

μg/liter) (19). The study sample was too small to definitively assess population iodine sufficiency (20), but the findings suggest that United States vegans may be at risk for iodine deficiency. Vegan diets do not contain dairy products and may be the reason for the vegans' lower urinary iodine levels, although it is reassuring that these were not associated with thyroid dysfunction.

Our findings are especially important to vegan and vegetarian women of child-bearing age (78% of the women in our study were between the ages of 15–44 yr, inclusive), in whom even mild iodine deficiency may have potential adverse effects during pregnancy and lactation. The American Thyroid Association has recommended that North American pregnant and lactating women receive prenatal vitamins containing 150 μg iodine daily (as potassium iodide) (21). Only 20.3% of pregnant and 14.5% of lactating women in the United States take an iodine-containing supplement (22). Currently 69% of prescription and 28% of nonprescription prenatal U.S. multivitamins contain iodine, many of which do not contain the labeled amount, especially when kelp is the iodine source (23, 24).

The median urinary perchlorate levels in our study are comparable with that of the general U.S. population (age 6 yr and older) (median 3.6 μg/liter; n = 2820) (16). There was no difference in median urinary perchlorate concentrations between vegetarians and vegans, and environmental perchlorate exposure was not associated with thyroid function. These results are consistent with other studies that reported a lack of correlation between urinary perchlorate levels and thyroid function: among men (25), women of child-bearing age using creatinine-adjusted urinary values from the 2001–2002 NHANES data set (26) and in a large European study assessing thyroid function of iodine-deficient pregnant women (27). However, the NHANES data showed that urinary perchlorate levels did adversely affect thyroid function in women with urinary iodine concentrations less than 100 μg/liter (25).

Only six subjects in each group were active recent smokers based on urine cotinine concentrations. Thus, smoking-generated thiocyanate cannot explain the higher thiocyanate levels in the vegans. The natural thiocyanate content in food is generally low, and consumption of these foods does not usually produce clinically significant sequelae unless severe iodine deficiency is also present.

The cross-sectional design of our study has limitations. Some subjects may regularly consume iodine-rich foods not recently ingested, thus resulting in lower spot urinary iodine measurements. The use of spot urine samples may have obscured the lack of correlation between urinary iodine levels and thyroid function because 12 or more spot urine samples are needed for precision within 20% (20). Potential misclassification of subjects' diets is possible, but confirmatory questioning of recent nonvegetarian or nonvegan intake was also obtained. Many of the vegetarians

TABLE 3. Concentrations [medians (range)] of urinary iodine, perchlorate, and thiocyanate and serum thyroid function of after exclusion of 12 subjects with elevated urinary cotinine levels

	Vegetarians (n = 72)	Vegans (n = 56)	*P*
Urinary iodine (μg/liter)[a]	141.8 (9.3–778.6)	78.5 (6.8–964.7)	<0.01
Urinary perchlorate (μg/liter)[a]	3.9 (0.2–42)	3.7 (0.3–258)	0.74
Urinary thiocyanate (μg/liter)[a]	321 (31–198)	576 (108–2563)	<0.01
Urinary cotinine (ng/ml)[a]	0.13 (0–80)	0.02 (0–244)	0.18
TSH (mIU/liter)[b]	1.39 (0–3.52)	1.08 (0.17–6.81)	0.34
FT4 (ng/dl)[b]	1.28 (0.95–1.66)	1.23 (0.92–1.67)	0.91

[a] n = 71 (vegetarians) and n = 56 (vegans) due to missing data.

[b] n = 70 (vegetarians) and n = 54 (vegans) due to missing data.

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were Asian, owing to the significant percentage of vegetarian Indians recruited.

Because the United States is considered to be iodine sufficient and the components of U.S. vegetarian and vegan diets may be variable, our data should be interpreted in context and may not be generalizable to individuals living in other regions. These results help to underscore the importance of identifying U.S. populations with possible low iodine intake and provide further understanding of whether environmental perchlorate and thiocyanate exposures adversely affect iodine nutrition and thyroid function in susceptible individuals.

Acknowledgments

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