Higher total homocysteine concentrations and lower folate concentrations in premenopausal black women than in premenopausal white women1–3


ABSTRACT

Background: Premenopausal black women have a greater rate of coronary artery disease (CAD) than do premenopausal white women. Plasma total homocysteine concentrations, a risk factor for CAD, have not been reported in premenopausal black women.

Objective: The purpose of this study was to compare plasma total homocysteine, folate, and vitamin B-12 concentrations in premenopausal black and white women.

Design: Eighty-nine black and 90 white, healthy, premenopausal women living in Portland, OR, were recruited. Dietary histories were obtained by using the Diet Habit Survey, a 40-item eating-behavior questionnaire. Plasma concentrations of total homocysteine, folate, and vitamin B-12 were measured.

Results: Black women had higher plasma total homocysteine (8.32 compared with 7.60 μmol/L; P = 0.013), lower plasma folate (6.62 compared with 9.88 nmol/L; P < 0.0001), and higher vitamin B-12 (355 compared with 283 pmol/L; P < 0.001) concentrations than white women. White women had a greater rate of daily multivitamin supplement use (42.4% compared with 24.7%; P = 0.019) and ate more ready-to-eat cereal than did black women. After adjustment for multivitamin use and intake of ready-to-eat cereal, plasma total homocysteine concentrations did not differ significantly, but plasma folate remained significantly lower in the black women. None of the black women but 12.3% of the white women (P = 0.013) were homozygous for the cytosine to thymidine mutation at nucleotide 677 in the methylenetetrahydrofolate reductase gene.

Conclusions: Black women had higher plasma total homocysteine and lower plasma folate concentrations than white women, largely because of lifestyle factors, which may contribute to the greater rate of CAD in premenopausal black than in white women.

KEY WORDS Homocysteine, folic acid, vitamin B-12, black women, white women, premenopause, coronary artery disease, multivitamins, ready-to-eat cereals, racial differences, methylenetetrahydrofolate reductase, MTHFR genotype

INTRODUCTION

Premenopausal black women have a 2–3-fold greater rate of coronary artery disease than do premenopausal white women (1–4). Increased rates of obesity (5) and hypertension (6) in black women likely contribute to their greater rate of coronary artery disease. Although plasma total and LDL-cholesterol concentrations are similar between the races (7), black women have higher HDL-cholesterol (8) and lower triacylglycerol (9) concentrations than white women. Thus, the overall lipoprotein profile is less, not more, atherogenic in black women. Although concentrations of plasma total homocysteine—an independent risk factor for coronary artery disease, stroke, and peripheral arterial disease (10–12)—have been reported in premenopausal white women (13), no studies have reported plasma homocysteine concentrations in premenopausal black women. If a racial disparity in plasma total homocysteine exists, it could contribute to the higher rate of coronary artery disease in premenopausal black than in white women.

The primary hypothesis of this study was that premenopausal black women have higher fasting plasma total homocysteine concentrations than comparable white women. Therefore, we compared plasma total homocysteine concentrations in a sample of healthy black and white premenopausal women. Plasma concentrations of folate and vitamin B-12, 2 vitamins that play an important role in homocysteine metabolism (11, 12, 14, 15), were also measured. In a subset of women, the methylenetetrahydrofolate reductase (MTHFR) genotype was determined. Dietary data and information concerning the use of multivitamin supplements were also collected.

1From the Division of Endocrinology, Diabetes, and Clinical Nutrition; the Division of Laboratory Medicine, Department of Pathology; and the Division of Hematology and Medical Oncology, Department of Medicine, General Clinical Research Center, Portland, OR; the Oregon Regional Primate Research Center, Beaverton, OR; and Oregon State University, Department of Nutrition and Food Management, Corvallis.

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3Address reprint requests to GT Gerhard, Department of Medicine, L465, Oregon Health Sciences University, 3181 SW Sam Jackson Park Road, Portland, OR 97201-3098. E-mail: gerhard@ohsu.edu.
HOMOCYSTEINE CONCENTRATIONS IN BLACK WOMEN

SUBJECTS AND METHODS

Subjects

One hundred black and 100 white premenopausal women aged 18–45 y were recruited, by using quota sampling, for participation in a study that examined racial differences in several coronary artery disease risk factors (16). Potential participants were considered black if they defined themselves as black. Complete data for plasma total homocysteine, folate, and vitamin B-12 were available in 89 black and 90 white women, who are the subject of this report. This study was approved by the Institutional Review Board at the Oregon Health Sciences University (OHSU). Women were recruited from OHSU employees, mothers of children attending the Albina Head Start school readiness program, Albina Head Start employees, and the general Portland, OR, community. Recruitment methods included advertisements in the OHSU campus newsletter, in Portland newspapers, and on the radio, and by word of mouth among Albina Head Start mothers and staff. All participants were healthy and had regular menstrual periods. Women with diabetes, who had renal or hepatic diseases, or who were currently abusing alcohol or illicit drugs were excluded. Written informed consent was obtained from all participants.

Methods

The evaluation procedure included a medical and dietary history and measurement of height, weight, and blood pressure. In addition, a venipuncture was conducted after a 12-h fast for determination of plasma total homocysteine, folate, and vitamin B-12 concentrations; MTHFR genotype; and concentrations of plasma creatinine, which may be correlated with fasting plasma total homocysteine concentrations (17). The dietary history was obtained by dietitians trained in using the Diet Habit Survey, a previously validated 40-item eating-behavior questionnaire developed at OHSU for assessment of dietary intake over the preceding month (18). Information was obtained about the intake of foods rich in folates, including fruit, vegetables, legumes, and especially ready-to-eat cereals (19). About 95% of ready-to-eat cereals are fortified with folic acid and most of these cereals provide 25% of the recommended dietary allowance (20) for folate per serving of cereal. The serving size for ready-to-eat cereals ranges from 0.12 to 0.24 L (0.5 to 1 cup). At the time our study was conducted, ready-to-eat cereals were, perhaps, the largest variety of foods rich in folates, including fruit, vegetables, legumes, and especially ready-to-eat cereals (19). About 95% of ready-to-eat cereals are fortified with folic acid and most of these cereals provide 25% of the recommended dietary allowance (20) for folate per serving of cereal. The serving size for ready-to-eat cereals ranges from 0.12 to 0.24 L (0.5 to 1 cup). At the time our study was conducted, ready-to-eat cereals were, perhaps, the largest variety of foods rich in folates, including fruit, vegetables, legumes, and especially ready-to-eat cereals (19). About 95% of ready-to-eat cereals are fortified with folic acid and most of these cereals provide 25% of the recommended dietary allowance (20) for folate per serving of cereal. The serving size for ready-to-eat cereals ranges from 0.12 to 0.24 L (0.5 to 1 cup). At the time our study was conducted, ready-to-eat cereals were, perhaps, the largest variety of foods rich in folates, including fruit, vegetables, legumes, and especially ready-to-eat cereals (19). About 95% of ready-to-eat cereals are fortified with folic acid and most of these cereals provide 25% of the recommended dietary allowance (20) for folate per serving of cereal. The serving size for ready-to-eat cereals ranges from 0.12 to 0.24 L (0.5 to 1 cup). At the time our study was conducted, ready-to-eat cereals were, perhaps, the largest variety of foods rich in folates, including fruit, vegetables, legumes, and especially ready-to-eat cereals (19).

Laboratory analyses

Plasma total homocysteine, folate, and vitamin B-12

Approximately 10 mL fasting venous blood was drawn into a tube containing EDTA as anticoagulant. The plasma was separated immediately by centrifugation (2000 × g, 10 min, 4°C) and stored at −80°C until analyzed. Plasma total homocysteine concentrations were determined by HPLC as described previously (34, 35). The interassay CV for the homocysteine assay was 9.1% (36). Plasma concentrations of folate and vitamin B-12 were measured by using the Quantaphase II B-12/folate radioassay kit provided by Bio-Rad Laboratories, Hercules, CA (37). The normal range for plasma folate with this method in our laboratory is 3.4–46.7 nmol/L (CV: 8.0%) and for vitamin B-12 is 96–568 pmol/L (CV: 6.8%).

MTHFR genotyping by polymerase chain reaction

Preliminary racial differences in plasma total homocysteine concentrations observed after the study began aroused our interest; therefore, the MTHFR genotype, which may be related to plasma total homocysteine concentrations (38), was determined in a subset of women (50 black and 57 white). DNA was extracted from frozen plasma by double phenol-chloroform extraction (AJ Evans, TG Deloughery, RD Press, unpublished observations, 1996) and the MTHFR genotype determined by using the polymerase chain reaction as described previously (38). The MTHFR genotype was classified as wild type (C677C: 2 cytosines at nucleotide 677), heterozygous (C677T: substitution of one of the cytosines with thymidine), or homozygous for the mutation (T677T: substitution of both cytosines with thymidine).

Plasma creatinine

The plasma creatinine concentration was determined by using the Jaffé rate method (39), a colorimetric procedure based on the formation of a red color complex on addition of the plasma sample to an alkaline picrate solution.

Statistical methods

A Kolmogorov-Smirnov test was used to determine whether the distribution of variables departed significantly from normality (40). Because the plasma total homocysteine, folate, and vitamin B-12 distributions were skewed, log10 transformations were performed on these variables. The log transformations improved normality in the homocysteine data and ameliorated the skewness in the folate and vitamin B-12 distributions. Statistical analyses were performed on the log-transformed variables and geometric means reported. Plasma total homocysteine, folate, vitamin B-12, and creatinine concentrations were compared between the races by using an unpaired t test (41). Dietary intakes of ready-to-eat cereals, fruit and vegetables, legumes, meat (including fish and poultry), cheese, and alcohol, as well as educational attainment (in y) and family income level were compared by using the Mann-Whitney rank-sum test (42) because these variables were not normally distributed and log transformation did not normalize...
the data. Thus, these variables are reported as medians. Least-squares linear regression (43) of log10 plasma total homocysteine on log10 plasma folate was performed to determine whether the relation between plasma total homocysteine and folate concentrations was similar or different between the races.

The chi-square test (42) was used to analyze categorical variables, including the percentage of black women compared with white women who had low or low-normal plasma folate concentrations, the percentage of black and white women taking a daily multivitamin supplement, and the race-specific prevalence of cigarette smoking. Multiple linear regression analysis (43) of daily multivitamin use (yes or no; dependent variable) on race, educational attainment, and income level (independent variables) was performed to determine the influence of socioeconomic status on multivitamin use in black and white women. A two-way analysis of variance procedure (multivitamin use by race) was performed on the log-transformed variables to ascertain the influence of multivitamin use on plasma total homocysteine, folate, and vitamin B-12 concentrations in both races (42). Spearman rank-order correlation coefficients (r) (42) were computed to test for a relation between meat and cheese intake and plasma vitamin B-12 concentrations.

Multiple linear regression analysis (43) of log10 plasma total homocysteine on race, log10 plasma folate, log10 plasma vitamin B-12, plasma creatinine concentration, current cigarette smoking (yes or no), alcohol intake, daily multivitamin use (yes or no), intake of ready-to-eat cereal, fruit and vegetable intake, and legume intake was used to determine factors predictive of plasma total homocysteine concentrations. To ascertain factors predictive of plasma folate concentrations, multiple linear regression analysis of log10 plasma folate on likely predictors was performed, including race, daily multivitamin use (yes or no), intake of ready-to-eat cereal, fruit and vegetable intake, legume intake, and current cigarette smoking (yes or no), and alcohol intake. The interaction of alcohol intake and race was included in the log10 plasma folate multiple regression model (40) to determine whether the relation between plasma folate concentrations and alcohol intake was similar between the races.

The distribution of MTHFR genotypes (wild type, heterozygous, or homozygous) was determined in a subset of 50 black and 57 white women and the distribution was compared by using the chi-square test. A chi-square test was also used to compare the C677T allele frequency between black and white women. Plasma total homocysteine and folate concentrations were compared between white and black women with the wild type MTHFR genotype by using an unpaired t test.

Two-tailed P values < 0.05 were regarded as significant. The statistical analyses were performed by using SIGMASTAT (version 1.0; Jandel Scientific Software, Rafael, CA) and the graphics displays were created with SIGMAPLOT (version 2.0; Jandel Scientific Software).

RESULTS

Clinical and demographic characteristics

There were no significant differences in age or educational attainment between black and white women (Table 1). The typical black and white women participating in our study had some college education. Both the white and the black women were better educated than comparably aged white and black women in Portland, OR (44), and in the United States as a whole (45). The combined family income levels did not differ significantly between the races, nor did the percentages of black and white women who were current cigarette smokers. The median alcohol intake was low and not significantly different between the races. Black women had a significantly higher mean body mass index and significantly higher systolic and diastolic blood pressures than white women.

Plasma total homocysteine, folate, and vitamin B-12

Plasma total homocysteine concentrations were significantly higher in black than in white women (Table 2). The black women had significantly lower plasma folate concentrations than the white women. A greater percentage of black (44.9%) than white (24.4%) women had low (≤3.4 nmol/L) or low-normal (3.4–5.9 nmol/L) plasma folate concentrations (P = 0.006). Least-squares linear regression analysis (Figures 1 and 2) indicated that the relation between plasma total homocysteine and folate did not differ significantly between black and white women. Vitamin B-12 concentrations were significantly higher in the black than in the white women.

Multivitamin use

A greater percentage (P = 0.019) of white (42.4%) than black (24.7%) women took a daily multivitamin supplement. The most frequently used brands of multivitamin supplements were Cen-

| TABLE 1 | Baseline characteristics of premenopausal black and white women1 |
|-----------------|-----------------|-----------------|
| | Black women (n = 89) | White women (n = 90) |
| Age (y) | 33.6 ± 7.4 | 34.7 ± 7.2 |
| Education (y)2 | 14 | 15 |
| Family income ($/y)2 | (9–21) | (8–21) |
| Current cigarette smokers (%) | 11 | 13 |
| Alcohol consumption (drinks/wk)2 | < 1 | < 1 |
| Body mass index (kg/m²) | 32.2 ± 9.4 | 29.2 ± 9.6 |
| Systolic blood pressure (mm Hg) | 125 ± 18 | 116 ± 13 |
| Diastolic blood pressure (mm Hg) | 79 ± 15 | 75 ± 11 |

1 SD, except where otherwise indicated.
2 Median; range in parentheses.
3 Significantly different from black women: 1P < 0.05, 2P < 0.0001.
trum (Lederle Consumer Health, Madison, NJ), One-A-Day (Bayer Corp, Morristown, NJ), and Theragran-M (Mead Johnson, Evansville, IN), each of which provided 400 mg folic acid, 6–9 μg vitamin B-12, and 2–3 mg vitamin B-6. No subject was consuming supplemental folic acid, vitamin B-12 or vitamin B-6 apart from the daily multivitamin supplement. In a multiple linear regression analysis of multivitamin intake (yes or no) on race, educational attainment in years, and income level, only race was a significant predictor of multivitamin use ($P = 0.039$).

Regular users of multivitamin supplements had significantly lower plasma total homocysteine concentrations than nonusers (Table 3). After adjustment for multivitamin use, plasma total homocysteine concentrations did not differ significantly between black and white women. Plasma folate concentrations were significantly higher in multivitamin supplement users than in nonusers and in white women than in black women in both categories of multivitamin use. There was no difference in vitamin B-12 concentrations between users and nonusers of multivitamin supplements.

**Dietary intakes**

The median intake of ready-to-eat cereals was significantly greater in white than in black women (Table 4). Median intakes of fruit and vegetables and of legumes did not differ significantly between the races. Black women consumed more meat, fish, poultry, and cheese than did white women. There was no correlation of plasma vitamin B-12 concentrations with meat and cheese intake in either race.

**Plasma creatinine**

The mean plasma creatinine concentration did not differ significantly between the races: $66.30 \pm 13.26 \mu mol/L$ (0.75 ± 0.15 mg/dL) in black women and $65.42 \pm 11.49 \mu mol/L$ (0.74 ± 0.13 mg/dL) in white women.

**Methylenetetrahydrofolate reductase genotype**

The distribution of MTHFR genotypes was significantly different between black and white women (Table 5). No black women were homozygous for the mutation. The frequency of the C677T allele was lower in black (16%) than in white (32%) women ($P = 0.011$). Because MTHFR genotype status determines plasma total homocysteine response to folate depletion (38), we examined plasma total homocysteine and folate concentrations in patients with the wild type MTHFR genotype. Black women with the wild type genotype had significantly higher mean plasma total homocysteine ($8.48$ compared with $6.98 \mu mol/L$; $P = 0.003$) and lower folate ($7.39$ compared with $11.85 \mu mol/L$; $P = 0.001$) concentrations than white women with the wild type genotype. Thus, when the MTHFR genotype was controlled for, the racial disparity in plasma total homocysteine and folate concentrations increased.

**Multiple linear regression analyses**

Multiple linear regression analyses were performed to ascertain factors predictive of plasma total homocysteine and folate concentrations and to elucidate reasons for the higher plasma total homocysteine and lower folate concentrations in black than in white women. Significant differences were found between black and white women in multivitamin use and intake of ready-to-eat cereal, so these variables were included in the regression models. Potential effect modifiers, including cigarette smoking, alcohol intake, plasma vitamin B-12 concentrations, plasma creatinine, fruit and vegetable intake, and legume intake were also included in the regression models. MTHFR...
genotype was not included as a possible predictor of plasma total homocysteine and folate concentrations because it was only determined in a subset of subjects.

Multiple linear regression analysis was carried out with \( \log_{10} \) plasma total homocysteine concentrations (dependent variable) on race, \( \log_{10} \) plasma folate, \( \log_{10} \) plasma vitamin B-12, plasma creatinine, current cigarette smoking (yes or no), alcohol intake, daily multivitamin use (yes or no), intake of ready-to-eat cereal, fruit and vegetable intake, and legume intake (independent variables). Only \( \log_{10} \) plasma folate was a significant predictor of the \( \log_{10} \) plasma total homocysteine concentration (\( P < 0.0001 \)). This regression model explained 26% of the variability in the \( \log_{10} \) plasma total homocysteine concentration (adjusted \( R^2 = 0.259 \)). A multiple linear regression analysis of \( \log_{10} \) plasma folate on race, daily multivitamin use (yes or no), intake of ready-to-eat cereal, fruit and vegetable intake, legume intake (independent variables). Only \( \log_{10} \) plasma folate was a significant predictor of the \( \log_{10} \) plasma total homocysteine concentration (\( P < 0.0001 \)). This regression model explained 26% of the variability in the \( \log_{10} \) plasma total homocysteine concentration (adjusted \( R^2 = 0.259 \)). A multiple linear regression analysis of \( \log_{10} \) plasma folate on race, daily multivitamin use (yes or no), intake of ready-to-eat cereal, fruit and vegetable intake, legume intake indicated that race (\( P = 0.004 \)), multivitamin use (\( P < 0.0001 \)), intake of ready-to-eat cereal (\( P < 0.0001 \)), and alcohol intake indicated that race (\( P = 0.004 \)), multivitamin use (\( P < 0.0001 \)), intake of ready-to-eat cereal (\( P < 0.0001 \)), and alcohol intake were significant predictors of \( \log_{10} \) plasma folate. In this regression model the interaction term alcohol use \( \times \) race was not a significant predictor of \( \log_{10} \) plasma folate, indicating that the relation between alcohol use and plasma folate was similar in black and white women. The multiple linear regression model explained 32% of the variability in the \( \log_{10} \) plasma folate concentration (adjusted \( R^2 = 0.318 \)).

DISCUSSION

The primary findings of this study were that premenopausal black women in the population studied had significantly higher concentrations of plasma total homocysteine and lower plasma folate concentrations than premenopausal white women. This was the first study to compare plasma total homocysteine concentrations in a sample of premenopausal black and white women. The higher plasma total homocysteine and lower folate concentrations in the black women were likely the result of their

TABLE 3

<table>
<thead>
<tr>
<th></th>
<th>Multivitamin use</th>
<th>No multivitamin use</th>
<th>( p^2 )</th>
<th>Race</th>
<th>Multivitamin use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Black women ( n = 22 )</td>
<td>White women ( n = 38 )</td>
<td>Black women ( n = 67 )</td>
<td>White women ( n = 52 )</td>
<td></td>
</tr>
<tr>
<td>Total homocysteine (( \mu \text{mol/L} ))</td>
<td>7.50 ± 2.09</td>
<td>6.58 ± 1.89</td>
<td>8.61 ± 3.05</td>
<td>8.45 ± 3.04</td>
<td>NS</td>
</tr>
<tr>
<td>Folate (nmol/L)</td>
<td>8.45 ± 6.80</td>
<td>12.89 ± 8.81</td>
<td>6.12 ± 4.26</td>
<td>8.11 ± 6.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vitamin B-12 (pmol/L)</td>
<td>387 ± 213</td>
<td>294 ± 158</td>
<td>315 ± 159</td>
<td>274 ± 125</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^1\)Geometric mean ± SD. There were no significant interaction effects by ANOVA.
\(^2\)Main effects by ANOVA.
lower intakes of folate-containing multivitamin supplements and ready-to-eat cereal compared with the white women. Premenopausal black women have a higher risk of coronary artery disease than do white women (1–4). Factors that may contribute to this increased risk include higher rates of obesity and hypertension and consumption of diets high in saturated fat and cholesterol (16). We identified plasma total homocysteine as an additional coronary artery disease risk factor, which is higher in premenopausal black than in white women. The plasma total homocysteine concentration is an independent risk factor for the development of coronary artery disease (46), cerebrovascular disease (47), and peripheral arterial occlusive disease (34). Homocysteine may increase cardiovascular risk through injury to vascular endothelial cells (48), leading to vascular dysfunction (49) and to other changes that promote both atherogenesis and thrombogenesis (48, 50). Cardiovascular risk increases across the spectrum of homocysteine concentrations (48, 50). Cardiovascular disease (47, 50), cerebrovascular disease (47), and peripheral arterial occlusion (50, 51) were associated with plasma total homocysteine concentration. In Boushey et al.’s (51) meta-analysis, a 5-μmol/L increment in the plasma total homocysteine concentration was associated with a 60% increased risk for coronary artery disease in men and an 80% increased risk in women. However, definitive proof of a cause-and-effect relation between plasma total homocysteine and coronary artery disease awaits the results of ongoing controlled intervention trials.

Three vitamins—folic acid, vitamin B-12, and vitamin B-6—play an important role in homocysteine metabolism (Figure 3). The folic acid derivative 5-methyltetrahydrofolate, produced by the enzymatic reduction of 5,10-methylenetetrahydrofolate by MTHFR, acts as a methyl donor in the remethylation of homocysteine to methionine (14). Vitamin B-12 is an essential cofactor for 5-methyltetrahydrofolate–homocysteine in the remethylation reaction (11, 12, 14, 15). Vitamin B-6, a necessary cofactor in the 2-step conversion of homocysteine to cysteine (14), plays an important role in determining the magnitude of the hyperhomocysteinemic response to a methionine load (14), but may be less important than plasma folate as a determinant of the fasting plasma total homocysteine concentration (52, 53).

In an important study of homocysteine metabolism in black and white South African men (54), black men showed a smaller hyperhomocysteinemic response to methionine loading but had fasting plasma total homocysteine concentrations similar to those of white men. It is difficult to compare our findings with those of the study of South African men because South African blacks differ genetically from American blacks (55, 56) and men rather than women were studied. Nevertheless, the South African data do indicate that, at least in South Africa, there may be genetic differences in homocysteine metabolism between blacks and whites that would not be reflected in their fasting plasma total homocysteine concentrations. These results must be interpreted with caution because of the relatively small sample size in that study (18 whites and 12 blacks).

As in our study, according to the 1987 National Health Interview Survey (57), a significantly greater percentage of white than of black women of reproductive age took a daily multivitamin supplement. In the National Health Interview Survey, daily multivitamin supplement use was strongly linked to socioeconomic status, which was not the case in our study. The racial difference in multivitamin supplement use we observed was possibly due to differences in unmeasured cultural or psychosocial factors that are not necessarily related to socioeconomic status (eg, unstable home environment and stress), which were associated with decreased vitamin intake in a prior study (58).

The black women in our study had a more marginal folic acid status than the white women, primarily because the black women had a lower rate of multivitamin use and lower intake of ready-to-eat cereals. Intakes of fruit and vegetables and legumes did not predict plasma folate concentrations. This may, in part, be secondary to a lower bioavailability of food folate than of synthetic folic acid in multivitamins and supplemented foods (59), which would lower the sensitivity of food folates as a predictor of plasma folate concentrations. In addition, the Diet Habit Survey does not differentiate between fruit and vegetables that are high or low in folates. The intake of alcohol, which interferes with folate utilization at multiple steps (22, 26), was a predictor of plasma folate in the multiple linear regression model, but did not contribute to the racial difference in plasma folate concentrations. In contrast with the findings of other studies (31, 32, 60), cigarette smoking was not associated with plasma folate concentrations in our study, although the power to detect an association was limited by the low number of smokers in both races. Even after all of these predictors were accounted for, however, race remained a significant predictor of plasma concentration.

TABLE 4

<table>
<thead>
<tr>
<th></th>
<th>Black women (n = 89)</th>
<th>White women (n = 90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ready-to-eat cereals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(L/wk)</td>
<td>0.24</td>
<td>0.55 (0–3.50)</td>
</tr>
<tr>
<td></td>
<td>(0–3.50)</td>
<td>(0–3.40)</td>
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<tr>
<td>(cups/wk)</td>
<td>1.0</td>
<td>2.3 (0–14.6)</td>
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<tr>
<td></td>
<td>(0–14.6)</td>
<td>(0–14.2)</td>
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<tr>
<td>Fruit and vegetables</td>
<td></td>
<td></td>
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<tr>
<td>(L/wk)</td>
<td>0.96</td>
<td>0.96 (0–3.80)</td>
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<tr>
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<td>(0–3.80)</td>
<td>(0–2.40)</td>
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<tr>
<td>(cups/wk)</td>
<td>4.0</td>
<td>4.0 (0–15.6)</td>
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<tr>
<td></td>
<td>(0–15.6)</td>
<td>(0–9.9)</td>
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<tr>
<td>Legumes</td>
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<tr>
<td>(L/wk)</td>
<td>0.24</td>
<td>0.24 (0–1.40)</td>
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<td></td>
<td>(0–1.40)</td>
<td>(0–2.90)</td>
</tr>
<tr>
<td>(cups/wk)</td>
<td>1.0</td>
<td>1.0 (0–5.8)</td>
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<tr>
<td></td>
<td>(0–5.8)</td>
<td>(0–12.1)</td>
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<tr>
<td>Meat (including fish, poultry, and cheese)</td>
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</tr>
<tr>
<td>(g/d)</td>
<td>200</td>
<td>129 (0 to &gt; 312)</td>
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<tr>
<td></td>
<td>(0 to &gt; 312)</td>
<td>(0 to &gt; 312)</td>
</tr>
<tr>
<td>(oz/d)</td>
<td>7.0</td>
<td>4.5 (0 to &gt; 11.0)</td>
</tr>
<tr>
<td></td>
<td>(0 to &gt; 11.0)</td>
<td>(0 to &gt; 11.0)</td>
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1 Median; range in parentheses; 2 significantly different from black women; 3 P = 0.007; 4 P = 0.004.

TABLE 5

<table>
<thead>
<tr>
<th></th>
<th>Black women</th>
<th>White women</th>
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</thead>
<tbody>
<tr>
<td>Wild type</td>
<td>34 (68.0)</td>
<td>27 (47.4)</td>
</tr>
<tr>
<td>Heterozygous</td>
<td>16 (32.0)</td>
<td>23 (40.3)</td>
</tr>
<tr>
<td>Homozygous</td>
<td>0 (0)</td>
<td>7 (12.3)</td>
</tr>
</tbody>
</table>

1 n; percentage in parentheses. There was a significant difference between black women and white women in the MTHFR distribution, P = 0.013 (chi-square test).
folate concentrations. Thus, other unmeasured variables possibly associated with race also contributed to the racial difference in plasma folate concentrations.

A common point mutation (cytosine to thymidine) at nucleotide 677 in the gene coding for the MTHFR enzyme results in a thermolabile variant of the enzyme with reduced basal activity (61). This mutation is associated with higher plasma total homocysteine concentrations at a given plasma concentration of folate (62), and, in addition, lowers plasma folate concentrations by decreasing the formation of 5-methyltetrahydrofolate, the primary circulating form of folic acid (38, 63). Thus, individuals homozygous for the MTHFR mutation have higher plasma total homocysteine concentrations (15, 61, 64) and are more sensitive to dietary folate depletion than are individuals without the mutation (38). Our study confirms earlier reports (15, 61–65) that the point mutation in the MTHFR gene is more common in white than in black women.

Finally, plasma vitamin B-12 concentrations were significantly higher in the black than in the white women. However, the higher plasma vitamin B-12 concentrations in the black women did not protect them from an increase in plasma total homocysteine concentrations associated with lower plasma folate concentrations. The higher meat and cheese intake of the black women was not the reason for their higher plasma total homocysteine concentrations associated with lower plasma folate concentrations. The higher meat and cheese intake of the black women was not the reason for their higher plasma vitamin B-12 concentrations because meat and cheese intake was not correlated with plasma vitamin B-12 concentrations.

One limitation of our study was that the Diet Habit Survey did not provide a precise measure of vitamin B-6 intake, although it did permit a comparison of the intakes of certain vitamin B-6–rich foods (eg, meat, beans, and fortified cereals) between the races (66). Black women had a higher intake of meat, and white women ate more fortified cereal, whereas the intake of beans was similar between the races. On balance, it is unlikely that dietary vitamin B-6 intakes differed substantially between black and white women. The amount of vitamin B-6 in the multivitamin supplements (2–3 mg) was unlikely to have had a significant effect on fasting plasma total homocysteine concentrations, as supported by the results of a previous study (67).

In conclusion, the higher plasma total homocysteine and lower folate concentrations in premenopausal black than in premenopausal white women in our study were primarily the result of lifestyle factors. Our data suggest that higher plasma total homocysteine concentrations may contribute to the greater rate of coronary artery disease in premenopausal black than in white women, although prospective clinical trials are needed to prove this hypothesis. If the hypothesis is correct, regular intake of multivitamin supplements or folic acid alone and increased intakes of ready-to-eat cereals may be a cost-effective means of attenuating the high risk of coronary artery disease in premenopausal black women.

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