CURRENT THERAPEUTIC RESEARCH
VOLUME 63, NO. 7, JULY 2002

Brief Report

Nutritional and Racial Determinants of the Increase in Plasma Homocysteine Levels After Methionine Loading

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ABSTRACT

Background: Low circulating plasma levels of total homocysteine (tHcy) are associated with a lower prevalence of coronary heart disease among black people than among white people living in Burkina Faso.

Objective: The purpose of this study was to provide a rationale for a possible mechanism for the decrease in plasma tHcy levels among black people compared with white people living in Burkina Faso.

Methods: Healthy, black, adult, lifelong inhabitants of Burkina Faso and healthy, white adults born in Italy but living in Burkina Faso ≥5 years were eligible for enrollment. Controlled diets were assigned to all subjects for 2 weeks before the study. After an overnight (12-hour) fast, a methionine-loading test was performed in all subjects. Plasma levels of tHcy, cysteine, glutathione, and cysteinylglycine were measured simultaneously using high-performance liquid chromatography after fasting (baseline) and at either 4 and 8 hours (n = 30) or 2, 4, 6, and 8 hours (n = 4) after methionine loading. During the 12 hours after loading, the clinical conditions and adverse events of subjects were monitored. Results were analyzed using the Student *t* test and Mann-Whitney *U* test.

Results: Seventeen black adults (9 males, 8 females; median age, 21 years) and 17 white adults (8 males, 9 females; median age, 35 years) were enrolled. Mean plasma levels of tHcy, cysteine, and glutathione increased from mean baseline levels more slowly in the black group than in the white group and peaked 8 hours after methionine loading (16.8 ± 3.0 μmol/L, 130.4 ± 25.7 μmol/L, and 68.3 ± 21.2 μmol/L, respectively). In the white group, these levels peaked 4 hours after loading (16.1 ± 4.0 μmol/L, 215.8 ± 18.6 μmol/L, and

Accepted for publication May 13, 2002.
 0011-393X/02/$19.00

38.6 ± 12.4 μmol/L, respectively). Only the mean plasma cysteinylglycine level decreased significantly (from 35.7 ± 11.4 μmol/L to 19.0 ± 6.1 μmol/L; $P < 0.01$) in the black group after 4 hours. This decrease was followed by an increase after 8 hours (29.6 ± 12.0 μmol/L). In the white group, a less remarkable change in mean cysteinylglycine level was observed, with a peak after 4 hours (16.3 ± 4.3 μmol/L).

Conclusions: The findings of this study suggest that, in addition to lower plasma tHcy levels, the metabolism of plasma tHcy is different in black people than in white people after methionine loading. This difference may be due to different alimentary habits associated with a reduced dietary availability of methionine. Moreover, the higher plasma levels of glutathione before and after methionine loading appear to occur exclusively in black people compared with whites and correspond with the variation of cysteinylglycine, suggesting that, in addition to nutritional factors, a racial component may contribute to the difference in plasma levels of tHcy. This difference also might explain, in part, the lower prevalence of coronary heart disease in black people living in Burkina Faso compared with that in other populations.

Key words: homocysteine, black people, methionine loading, Burkina Faso. (*Curr Ther Res Clin Exp.* 2002;63:459–473)

INTRODUCTION

A study[1] carried out on a sample of black children and adults living in Burkina Faso has demonstrated that plasma total homocysteine (tHcy) levels are lower in black people than in white people living there, and also that plasma levels of tHcy are particularly low in black females, both as adults and children. These findings suggest a racial factor for tHcy level, although environmental and dietary influences on homocysteine metabolism have not been ruled out. This racial factor could be linked to diet: local, traditional meals for blacks and European-style meals for whites. Indeed, black individuals living in the United States and fully adapted to occidental habits show levels of tHcy comparable to those of white populations.[2,3] On the contrary, the plasma tHcy concentrations were significantly lower in black men living traditionally in South Africa and having a low prevalence of coronary heart disease than in white men.[4] After oral methionine loading in these black men, a more effective homocysteine metabolism was found, which correlates well with a possible explanation about the lower prevalence of coronary heart disease in these subjects,[5] whereas white individuals with an elevated risk for cardiovascular diseases showed higher plasma tHcy concentrations after oral methionine loading.[6]

It also has been found that low baseline plasma levels of tHcy are associated with hyperhomocysteinemia after methionine-loading tests in individuals with high levels of serum and red blood cell folate,[7] confirming that the response to the methionine-loading test is related to sex-specific factors[8] and to metabolic modulation due to hormonal influences.[9]

The purpose of this study was to provide a rationale for a possible mechanism for the lower plasma tHcy levels among black people compared with white people living in Burkina Faso.

SUBJECTS AND METHODS

Healthy, black and white adults were enrolled in this study. Health was determined using laboratory tests as described later. For eligibility, all black subjects, of Mossi race, were born in Ouagadougou, Burkina Faso, and had lived in the same town since their birth. On the other hand, the white subjects were born in Italy and had been living in Ouagadougou for ≥5 years. All subjects were employees at the Medical Center of San Camille (MCSC). The social status of the black and white subjects was similar.

All eligible subjects were healthy, with no anamnestic pathologic conditions in the 6 months before the study began. Subjects' health was assessed before enrollment using subject visits, during which histories were taken. Blood was sampled for levels of plasma hemoglobin, glucose, and blood urea nitrogen and serum cholesterol, triglycerides, creatinine, iron, aminotransferases, folate, and vitamin B_{12}. Hemoglobin electrophoresis and red blood cell glucose-6-phosphate dehydrogenase determinations also were included in the panel of laboratory tests used to determine eligibility. Normal laboratory test values were those within 2 SD; subjects with a variation of these parameters >2 SD were not eligible for the study. People receiving anticonvulsive therapy and alcoholic individuals (ie, 2–3 drinks per day) were excluded.

All subjects gave written informed consent according to the principles of the Declaration of Helsinki. The protocol of this study was reviewed and approved by the ethics committee at MCSC.

In the 2 weeks before the study began, a controlled diet of 1.8 kcal/d was assigned to all participants, ensuring the similarity of caloric intake of all participants. Similarity of caloric intake of all subjects also was controlled using food diaries. Subjects' diets were typical of the traditions of their countries of origin. The black subjects typically ate millet or sorghum flour with vegetable sauce and cereals; chicken, pork, mutton, or beef (no fish) once a week; and local, in-season fruits. They did not include fonio (*Digitaria exilis*) in their diets. The Mediterranean diets of the white subjects typically included pasta and tomato sauce; daily beef or pork, except rice and fish once a week; cooked vegetables; and local, in-season fruits.

All of the pathologic conditions associated with a sizable increase in plasma tHcy level[6] (ie, a low level of folate or vitamin B_{12}, hypertension, atherothrombotic cardiovascular disease, diabetes, renal and hepatic diseases) were ruled out in all individuals by using the routine laboratory tests that were performed before enrollment. After enrollment, subjects completed a clinical form comprehensive of all parameters proving healthy status and organ function. Body weight, height, blood pressure, heart rate, and ventilation rate were measured

during the subject visits, and electrocardiography was performed by a cardiologist (S.P.). Body mass index (BMI) was calculated in all subjects.

Subjects fasted overnight (12 hours) before the oral methionine-loading test[7] was performed. On the day of the study, a venous blood sample with ethylenediaminetetraacetic acid was drawn by one of the authors (S.M.) as a baseline sample for all subjects. L-Methionine (mean dose, 100 mg/kg body weight), dissolved in 200 mL of orange juice, was administered orally by the same author (S.M.). Blood samples used to measure plasma levels of methionine, tHcy, cysteine, glutathione, and cysteinylglycine were drawn at either 4 and 8 hours or 2, 4, 6, and 8 hours after methionine loading. All blood samples were chilled, and plasma and cells were centrifuged (1500*g* for 10 minutes at 4°C) within 1 hour. The plasma samples and the packed cells were stored at −80°C and carefully shipped in dry ice to the Department of Pediatrics, University of Catania, Catania, Italy, where plasma tHcy, cysteine, cysteinylglycine, and glutathione levels were measured simultaneously with isocratic high-performance liquid chromatography and fluorescence detection ($\lambda ex = 385$ nm, $\lambda em = 515$ nm).[10] The plasma methionine level was measured in the laboratory by one of the authors (C.M.) using chromatography with sulfonated polystyrene resin.[11]

During the 12 hours after loading, the clinical conditions and adverse events of subjects were monitored by one of the authors (S.M.). All subjects were allowed water and noncarbonated soft drinks during the test period. After the last blood sample was taken (8 hours), subjects received dinner according to their ethnic tradition.

Statistical Analysis

The results of this study are expressed as mean ± SD or as median and range. The SD of the data of the 2 groups (black and white) were analyzed using the Student *t* test, taking unequal variances into account (Levin's test) when necessary. Because of the small size of the groups, the results also were confirmed with the Mann-Whitney *U* test. Statistical significance was set at $P \leq 0.05$.

RESULTS

Seventeen black adults (9 males, 8 females) aged 17 to 50 years (median, 21 years) and 17 white adults (8 males, 9 females) aged 28 to 39 years (median, 35 years) were enrolled. The black individuals conformed to the lifestyle and habits of their own ethnicity and were working at MCSC as waiters, cooks, and students. The white subjects were clerics, physicians, laboratory technicians, and voluntary collaborators at MCSC. Although most subjects underwent blood sample collection at 4-hour intervals after methionine loading (n = 30), 2 black subjects and 2 white subjects underwent blood sample collection at 2-hour intervals.

Table I reports the clinical and laboratory characteristics of the subjects, grouped according to race. The 2 groups did not show any significant

Table I. Clinical and laboratory parameters of black and white subjects (N = 34).

Parameter	Black Group (n = 17)	White Group (n = 17)
Sex, no.		
Male	9	8
Female	8	9
Age, y*	21 (17–50)	35 (28–39)
Body mass index, kg/m^{2}†	25.2 ± 1.4 (22–28)	26.4 ± 1.1 (22–29)
Plasma levels†		
Hemoglobin, g/dL	14.2 ± 2 (11–16)	15.5 ± 2 (11–17)
Glucose, mg/dL	84 ± 12 (70–96)	86 ± 9 (70–95)
Blood urea nitrogen, mg/dL	28 ± 6 (18–40)	27 ± 7 (19–41)
Serum levels†		
Cholesterol, mg/dL	176 ± 64 (120–240)	194 ± 66 (130–250)
Triglycerides, mg/dL	96 ± 9 (55–100)	101 ± 5 (60–108)
Creatinine, mg/dL	0.8 ± 0.1 (0.6–1.1)	0.8 ± 0.1 (0.6–1.2)
Iron, μg/dL	83 ± 22 (60–110)	97 ± 28 (45–116)
Aspartate aminotransferase, U/L	20 ± 5 (18–32)	21 ± 4 (19–33)
Alanine aminotransferase, U/L	22 ± 10 (19–35)	22 ± 9 (19–34)
Folate, ng/mL	15 ± 5 (8–19)	13 ± 4 (9–18)
Vitamin B_{12}, ng/mL	423 ± 38 (250–460)	417 ± 42 (260–450)
G6PD level, U/g Hb†	10 ± 3 (5–13)	11 ± 2 (5–13)
Systolic blood pressure, mm Hg†	132 ± 4 (105–135)	131 ± 8 (102–138)
Diastolic blood pressure, mm Hg†	82 ± 3 (69–89)	83 ± 2 (40–85)

G6PD = glucose-6-phosphate dehydrogenase.
*Values are expressed as median (range).
†Values are expressed as mean ± SD (range).

difference in baseline laboratory test parameters. The mean BMIs were 25.2 ± 1.4 kg/m^2 in the black group and 26.4 ± 1.1 kg/m^2 in the white group. Body weight, height, blood pressure, heart rate, and ventilation rate were in the normal range for age in all subjects.

The mean plasma levels of methionine, tHcy, cysteine, glutathione, and cysteinylglycine of the 4 subgroups (black men, black women, white men, white women) at baseline and at 4 and 8 hours after methionine loading are shown in Table II. The plots of the plasma methionine concentration and of the plasma levels of tHcy, cysteine, glutathione, and cysteinylglycine of subjects who underwent blood sample collection at 4-hour intervals are shown in Figure 1A to 1E. The plots of methionine and plasma tHcy levels of the subjects who underwent blood sample collection at 2-hour intervals are shown in Figure 1F and 1G.

In black subjects, the mean plasma methionine concentration peaked after 4 hours (94.6 ± 26.4 μmol/L) and decreased after 8 hours (59.4 ± 16.1 μmol/L). Mean plasma levels of tHcy, cysteine, and glutathione increased from mean baseline levels more slowly in the black group than in the white group.

Table II. Mean levels* (μmol/L) of methionine, total homocysteine (tHcy), cysteine, glutathione, and cysteinylglycine in subjects (N = 34) at baseline and 4 and 8 hours after methionine loading.

Level	Baseline	4 Hours	8 Hours
Black men (n = 9)			
Methionine	19.9 ± 6.0†	95.5 ± 19.0†	62.3 ± 11.5
tHcy	6.9 ± 1.3†	13.7 ± 1.7†	17.1 ± 2.2
Cysteine	96.3 ± 13.0	82.5 ± 14.1†	130.0 ± 21.2
Glutathione	43.3 ± 7.5	42.0 ± 10.1†	74.5 ± 16.7
Cysteinylglycine	37.1 ± 10.0†	22.4 ± 6.4	32.0 ± 10.2
Black women (n = 8)			
Methionine	21.9 ± 7.1†	103.0 ± 21.1†	63.3 ± 10.8
tHcy	5.9 ± 1.9†	12.7 ± 2.1†	15.1 ± 3.6
Cysteine	95.0 ± 14.4‡	68.3 ± 18.3†	127.1 ± 20.4
Glutathione	42.0 ± 9.5	39.3 ± 12.5‡	68.0 ± 21.3
Cysteinylglycine	34.3 ± 12.9‡	17.3 ± 5.7	29.0 ± 14.6
White men (n = 8)			
Methionine	20.9 ± 1.7†	95.4 ± 23.1‡	58.6 ± 10.0
tHcy	10.8 ± 0.6†	16.4 ± 1.0†	12.2 ± 1.6
Cysteine	134.3 ± 9.3†	215.0 ± 14.7†	181.4 ± 15.5
Glutathione	20.7 ± 1.5‡	39.0 ± 12.1†	17.3 ± 1.6
Cysteinylglycine	16.0 ± 2.0	16.7 ± 2.4	14.3 ± 1.7
White women (n = 9)			
Methionine	20.4 ± 1.1†	90.9 ± 16.8†	63.9 ± 9.2
tHcy	9.5 ± 1.5†	17.2 ± 3.3‡	13.6 ± 1.2
Cysteine	131.9 ± 12.5†	216.5 ± 23.1‡	186.9 ± 17.5
Glutathione	20.9 ± 1.6†	41.5 ± 9.6†	17.5 ± 1.8
Cysteinylglycine	16.0 ± 2.6	17.5 ± 3.4	13.4 ± 0.6

*Values are expressed as mean ± SD.
†$P < 0.001$.
‡$P < 0.01$.
Note: *P* values are comparisons between levels at baseline and at 4 and 8 hours after methionine loading in each of the 4 subgroups as determined using Student *t* test and Mann-Whitney *U* test. Nonsignificant *P* values are not shown.

In the black group, the mean plasma tHcy levels slowly increased, peaking after 8 hours (16.8 ± 3.0 μmol/L). In black subjects who underwent blood sample collection at 2-hour intervals after methionine loading, the peak of plasma methionine concentration was reached after 4 hours (99.5 ± 8.5 μmol/L), whereas the mean plasma tHcy level peaked after 8 hours (17.4 ± 0.7 μmol/L). After 24 hours, the tHcy plasma level returned to the mean baseline level (6.5 ± 1.8 μmol/L).

In the black group, the mean plasma cysteine level was stable or slightly decreased from baseline (22.6 ± 19.2 μmol/L) after 4 hours (17.6 ± 13.7 μmol/L), followed by a slight increase after 8 hours (30.4 ± 25.7 μmol/L). The mean

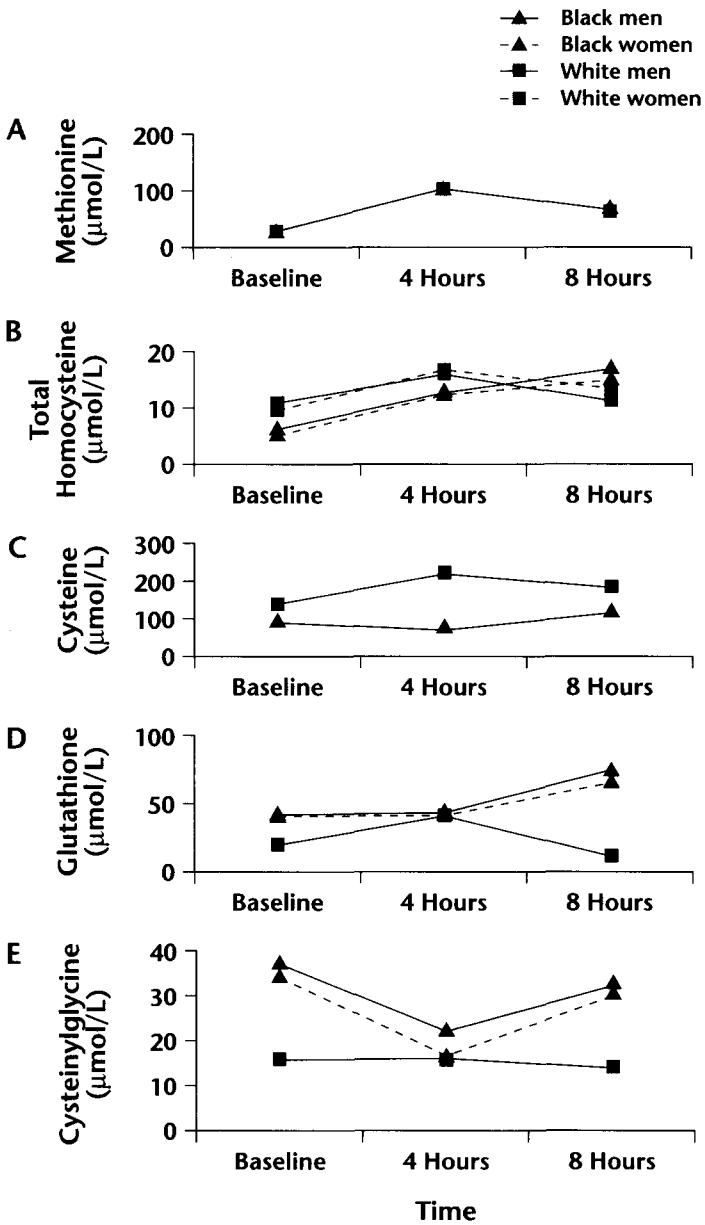

Figure 1. Curves of plasma levels of (A) methionine, (B) total homocysteine, (C) cysteine, (D) glutathione, and (E) cysteinylglycine at 4-hour intervals.

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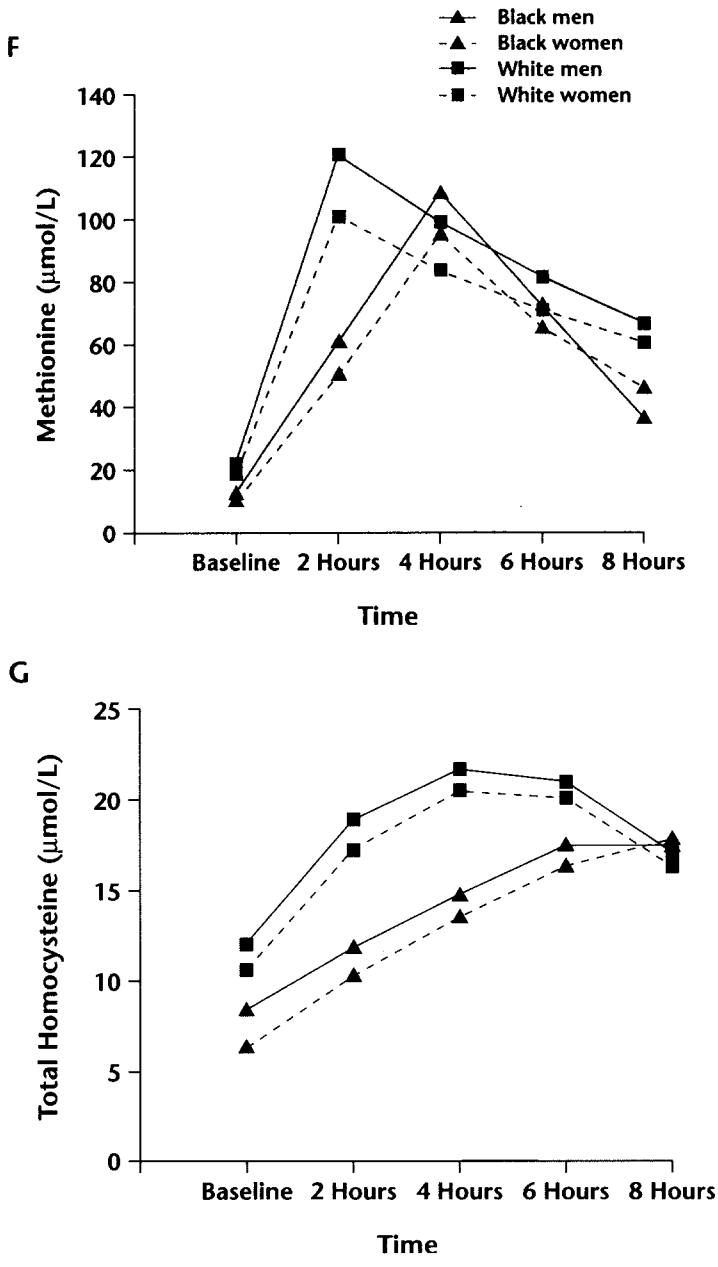

Figure 1. (continued.) Curves of plasma levels of (F) methionine and (G) homocysteine at 2-hour intervals.

plasma glutathione level was elevated (40.7 ± 11.1 μmol/L) compared with that of the white group at baseline (20.8 ± 1.6 μmol/L), remained stable after 4 hours (39.0 ± 12.3 μmol/L), and peaked after 8 hours (68.3 ± 21.2 μmol/L). The mean plasma cysteinylglycine level, which was elevated (35.7 ± 11.4 μmol/L) compared with that of the white group (16.0 ± 2.3 μmol/L) at baseline, decreased significantly after 4 hours (19.0 ± 6.1 μmol/L; $P < 0.01$) and increased after 8 hours (29.6 ± 12.0 μmol/L).

In the white group, the mean plasma methionine level from baseline (19.4 ± 4.9 μmol/L) peaked after 4 hours (88.4 ± 25.9 μmol/L) and decreased after 8 hours (58.5 ± 15.6 μmol/L; Figure 1A). The curves of the plots of the mean plasma tHcy, cysteine, glutathione, and cysteinylglycine levels show similar trends, with peaks after 4 hours (16.1 ± 4.0 μmol/L, 215.8 ± 18.6 μmol/L, 38.6 ± 12.4 μmol/L, and 16.3 ± 4.3 μmol/L, respectively) followed by statistically significant decreases after 8 hours ($P < 0.01$ for all). In the white subjects who underwent blood sample collection at 2-hour intervals after methionine loading, the mean plasma methionine level peaked after 2 hours (110.0 ± 14.1 μmol/L), whereas the mean plasma tHcy level peaked after 4 hours (21.2 ± 0.7 μmol/L).

The comparison of glutathione and cysteinylglycine plots in the black group shows that the mean plasma glutathione level increased after 8 hours (from the baseline level of 40.7 ± 11.1 μmol/L to 68.3 ± 21.2 μmol/L), whereas the mean plasma cysteinylglycine level decreased after 4 hours (from 35.7 ± 11.4 μmol/L to 19.0 ± 6.1 μmol/L).

Tolerance of methionine loading was different between the 2 groups. All white subjects manifested adverse events within the first 4 hours after methionine loading, including nausea (15 subjects), headache (5), and vomiting (3). Five white subjects lost time from work due to adverse events. On the other hand, all black subjects showed tolerance to methionine loading, with no adverse events or time lost from work reported.

DISCUSSION

Within the past 5 years, evidence has suggested that hyperhomocysteinemia may represent a risk factor for neural tube defect, arterial cardiovascular disease, and venous thrombosis.[12,13] Hyperhomocysteinemia may be related to a congenital metabolic defect[14] or acquired deficiency of folate, vitamin B_6, or vitamin B_{12}.[15] This evidence is supported by the consideration that disrupted sulfur amino acid metabolism determines an increase in plasma tHcy, which impairs the endothelium-dependent vasodilation affecting the vascular wall structure with both oxidant damage of low-density lipoprotein and superoxide production, which in turn stimulates smooth muscle cell proliferation[16] and interferes with the coagulation and fibrinolytic systems through activated protein C resistance.[17]

The methionine-loading test has been widely used to reveal impaired methionine/homocysteine metabolism and, in particular, the transsulfuration pathway.[7] This test sharply increases plasma tHcy levels enough to induce endo-

thelial dysfunction, but folate therapy decreases tHcy levels, restores endothelial function, and prevents oxidative damage.[18] Vitamins and folate, cofactors of key enzymes in homocysteine metabolism, may be administered, alone or in association with the treatment of hyperhomocysteinemia. However, there is no evidence that these vitamins improve the metabolism of homocysteine or reduce the risk for cardiovascular disease.[19]

Ubbink et al[5] measured in 18 white and 12 black volunteers the plasma tHcy level before and after 6 weeks of vitamin supplementation (1.0 mg of folic acid, 400 μg of vitamin B_{12}, and 10 mg of vitamin B_6) and found a reduction in mean plasma tHcy level from 9.6 ± 3.5 μmol/L to 7.2 ± 1.6 μmol/L ($P < 0.05$) and from 8.4 ± 2.4 μmol/L to 5.6 ± 1.4 μmol/L ($P < 0.01$), respectively. When methionine loading was performed in the same white volunteers, the plasma tHcy level decreased after vitamin supplementation from 18.0 ± 6.2 μmol/L to 11.1 ± 2.3 μmol/L, whereas vitamin supplementation did not have a significant effect on plasma tHcy level in black volunteers undergoing methionine loading. These observations demonstrate that plasma tHcy levels after methionine loading are not influenced by vitamin and folic acid supplementation in black people.

Experimental studies[20] in rats have demonstrated that a methionine-rich diet induces more efficient homocysteine metabolism, suggesting that humans, who have a variable methionine content in their diets, might respond differently to the methionine-loading test. However, Andersson et al[21] performed methionine loading in 6 healthy, white subjects before and after 2 weeks of excessive daily methionine intake (300% of the normal diet) and found that neither the methionine clearance rate nor the plasma tHcy level, measured at several intervals after methionine loading, was affected by excess methionine.

In the present study, the 2 groups had a similar socioeconomic status and worked in the same medical center, but their diets differed significantly. In fact, the diets of black people living in Burkina Faso consist mostly of flour of millet, sorghum, and rarely fonio. Fonio has the highest content of methionine plus cysteine (84 mg/g of protein[22]; Table III) compared with other cereals, but it was not introduced into the diets of the subjects in this study and does not influence homocysteine metabolism. The elevated content of tannins in millet and sorghum, however, reduced the availability of methionine in animal models in some studies.[23,24]

A similar mechanism that reduces the methionine availability and subsequently plasma tHcy levels cannot be ruled out in the black subjects in this study, who had consumed a diet based on millet and sorghum flours since infancy. This alimentation is different from that of the white subjects, whose diet was based mostly on wheat flour. The different flour contents in the diets of these 2 groups may have been the reason that the plasma methionine level in whites peaked 2 hours after loading and the plasma tHcy, cysteine, and glutathione levels peaked after 4 hours, compared with blacks, in whom these levels peaked after 8 hours.

Table III. Composition of different types of flour used for human alimentation.[22]

Composition	Millet	Sorghum	Fonio	Maize	Wheat
Proteins, g/100 g	9.7	10.1	7.9	9.5	9.2
Amino acids, mg/g proteins					
Isoleucine	41	39	40	37	35
Leucine	96	133	98	125	64
Lysine	34	20	56	27	18
Methionine + cysteine	48	29	84	35	37
Phenylalanine + tyrosine	80	76	87	87	68
Threonine	39	30	40	36	24
Tryptophan	19	12	14	7	9
Valine	55	50	58	48	38
Histidine	24	21	21	27	19

Our data for white subjects differ from those of Ubbink et al,[5] who found that in white subjects plasma tHcy levels measured after 8 hours were equal to or slightly higher than those measured after 4 hours, similar to the levels in the black people we studied. We think that this difference may have been the result of the different modalities of subject enrollment. In fact, in the study by Ubbink et al,[5] black and white subjects had the same lifestyles during the study (during the study period they lived under very similar conditions, sharing the same quarters and occupations). Most of their daily food intake was derived from the same college kitchen and included the same foods: cereals, chicken, pork, and in-season fruit. On the other hand, the 2 groups in our study consumed different diets. The methionine introduced by diet in the black group came essentially from cereals (flour of millet and sorghum) compared with the methionine given to the white group, which came from meat, milk, and cheese; only a small quantity of methionine in the white group came from cereals. Consequently, the different bioavailability of methionine coming from cereals compared with that from animal products may improve the tolerability of methionine loading in black subjects, who did not report any adverse events, compared with white subjects, who reported nausea, vomiting, and headache.

In blacks, the elevated content of tannins in the diet[23,24] appears to play an important role in the tolerability of methionine loading and could protect the endothelial tissue from the damage induced by elevated plasma tHcy levels.[25] This protective effect also may be synergic with the poor and uniform diet of the black population living in Burkina Faso.

Regarding the increase of plasma tHcy level with methionine loading, genetics, sex, age, and diet might be important, but habits such as smoking and coffee ingestion might be cultural determinants.[8] In fact, 1 study[26] that compared a black population living in the United States for several years with black West African inhabitants showed that the US blacks had a rich diet and lifestyle

that were similar to those of whites and that plasma tHcy levels were comparable in both groups. These results suggest that, aside from race, dietary factors and lifestyle habits may influence circulating plasma tHcy levels and consequently the effect on the cardiovascular system.

The correlation between plasma tHcy level and cardiovascular disease is apparent only in retrospective[27] rather than prospective studies. Whether a strict causal relationship exists remains undetermined; further studies are needed.

In the present study, we observed that the mean plasma glutathione level in the black group was roughly 4-fold that in the white group both before and after methionine loading. This result could be a consequence of a selective pressure on glutathione metabolism caused by malaria,[28] an endemic disease in Burkina Faso.[29]

Moreover, the mean plasma cysteinylglycine (a product of the breakdown of glutathione) level decreased at 4 hours and increased at 8 hours after methionine loading in black subjects. These results could be a consequence of the fact that methionine loading reduces the plasma glycine level through the relative inhibition of the folate cycle (serine vs glycine); this reduced level can be returned to normal in black individuals, but not in whites, by using cysteinylglycine hydrolysis (Figure 2).[30]

In addition, in the black group, 8 hours after methionine loading, the mean plasma methionine level had returned to the mean baseline level, and the low mean level of cysteinylglycine had increased to the mean baseline level. Similarly, the mean plasma glutathione and tHcy levels continued to increase and peaked after 8 hours. Also, the mean plasma levels of tHcy and glutathione were substantially higher after 8 hours in the black group than in the white group, in whom they returned to mean baseline levels after 8 hours. This paradoxical occurrence may have resulted from a slower methionine metabolism in blacks compared with whites, as was shown in subjects who underwent blood sampling at 2-hour intervals after methionine loading.

CONCLUSIONS

The findings of this study suggest that, in addition to lower plasma tHcy levels, the metabolism of plasma tHcy is different in black people than in white people after methionine loading. This difference may be due to different alimentary habits associated with a reduced dietary availability of methionine. Moreover, the higher plasma levels of glutathione before and after methionine loading appear to occur exclusively in the black group and correspond with the variation of cysteinylglycine, suggesting that, in addition to nutritional factors, a racial component may contribute to the difference in plasma levels of tHcy. This difference also might explain, in part, the lower prevalence of coronary heart disease in black people living in Burkina Faso compared with that in other populations.

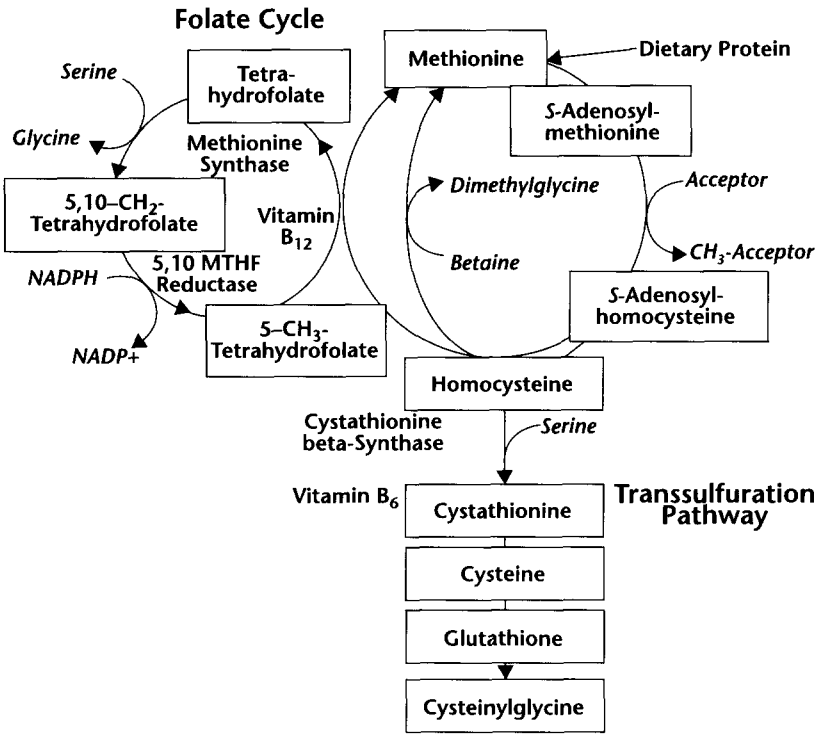

Figure 2. Homocysteine cycle.[30]

ACKNOWLEDGMENTS

The authors gratefully acknowledge the Department of Chemical Sciences, University of Catania, Catania, Italy, for their hospitality regarding our activities in the present study. Professor Sebastiano Sciuto is similarly acknowledged for his suggestions and constant help in the preparation of this article. Finally, all those who helped and made this study feasible are gratefully thanked.

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