DASH Diet Lowers Blood Pressure and Lipid-Induced Oxidative Stress in Obesity

Heno F. Lopes, Kelley L. Martin, Khaled Nashar, Jason D. Morrow, Theodore L. Goodfriend, Brent M. Egan

Abstract—Evidence suggests that obesity may raise blood pressure (BP) through oxidative stress–sensitive mechanisms and that the Dietary Approaches to Stop Hypertension combination diet (DASH-CD) may decrease BP by enhancing antioxidant capacity. To address this question, 12 obese patients with high-normal–to–stage 1 hypertension (hypertensives) and 12 lean normotensives were studied on their usual diets and after following the DASH-CD and a low-antioxidant diet in random sequence for 4 weeks each. Acute oxidative stress was induced by a 4-hour infusion of intralipid and heparin. Ferric-reducing activity of plasma (FRAP) and plasma F₂-isoprostanes were measured as biomarkers of antioxidant capacity and oxidative stress, respectively. BP was lower in obese hypertensives on the DASH-CD than on the usual and low-antioxidant diets (−8.1±1.5/−7.4±1.6 mm Hg, P<0.05). BP did not change significantly in lean normotensives after 4 weeks on the DASH-CD but tended to rise on the low-antioxidant diet. FRAP on usual diets was higher in lean subjects than in obese subjects. FRAP increased in obese but not lean volunteers on the DASH-CD compared with usual diet, and the group difference disappeared. F₂-isoprostanes increased from baseline during intralipid and heparin in both groups on the low-antioxidant diet but not in obese hypertensives on the DASH-CD. Among free-living obese hypertensives, the DASH-CD raises antioxidant capacity, lowers BP, and reduces oxidative stress induced by acute hyperlipidemia. The findings are consistent with evidence that elevated BP in obese subjects may reflect an imbalance between antioxidant capacity and oxidative stress that is improved by the DASH-CD.

Key Words: obesity ■ insulin resistance ■ fatty acids ■ F₂-isoprostanes ■ oxidative stress ■ antioxidants

Patients with high-normal blood pressure (BP) and hypertension are more obese and insulin resistant than are normotensives. Reduced antioxidant capacity and oxidative stress represent a potential mechanism linking obesity with insulin resistance, elevated BP, and cardiovascular disease.1–10 For example, acutely raising lipids with a short-term infusion of intralipid and heparin, which mimics and/or exacerbates the dyslipidemia seen with insulin resistance, increases BP and raises F₂-isoprostanes, a biomarker of oxidative stress.11,12 Moreover, in experimental models, increasing oxidative stress with a long-term low-dose infusion of angiotensin and reducing antioxidant capacity by depletion of glutathione produce severe hypertension.2,13 In these models, BP declines when antioxidant defenses are augmented by providing either superoxide dismutase13,14 or vitamins C and E.13 Vitamin C also lowers BP in humans, which implicates a role for antioxidant capacity in human hypertension.15

In the Dietary Approaches to Stop Hypertension (DASH) Study, a diet rich in fruits and vegetables, either with or without low-fat dairy products, reduced BP significantly more in hypertensives than in normotensives.16 Both diets are rich in a variety of antioxidants, which may contribute to the BP-lowering effects. Collectively, published observations raise the possibility that the DASH intervention lowers BP by increasing antioxidant capacity, particularly in obese insulin-resistant hypertensives. The principal focus of the present study was to determine the impact of the DASH prescription on BP and indices of antioxidant capacity and oxidative stress at baseline and in response to an acute lipid stressor in free-living obese subjects with high-normal and stage 1 hypertension (hypertensives) and lean normotensive volunteers.

Methods

Human Volunteers

All subjects read and signed a written informed consent document approved by the Institutional Review Board and the General Clinical Research Center (GCRC) Advisory Committee. Twenty-four volunteers were enrolled, including 12 obese (body mass index ≥27

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From the Departments of Pharmacology (H.F.L., K.N., B.M.E.) and Medicine (B.M.E.) and the General Clinical Research Center (K.L.M., B.M.E.), Medical University of South Carolina, Charleston; Unidade de Hipertensão-Heart Institute (InCor), HCFM-USP (H.F.L.), São Paulo, Brazil; Departments of Pharmacology and Medicine, Vanderbilt University School of Medicine (J.D.M.), Nashville, Tenn; and Departments of Pharmacology and Medicine, University of Wisconsin and William S. Middleton Veterans Hospital (T.L.G.), Madison.

Correspondence to Brent M. Egan, MD, Departments of Medicine and Pharmacology, Medical University of South Carolina, 96 Jonathan Lucas St, CSB 826H, Charleston, SC 29425, E-mail eganbm@musc.edu

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kg/m²) dyslipidemic (triglycerides >150 mg/dL and/or HDL-cholesterol <45 for women or <40 mg/dL for men) subjects with high-normal to stage 1 hypertension (BP 130 to 159/85 to 99 mm Hg) and 12 lean (body mass index ≤25 kg/m²) normotensives (BP <130/85 mm Hg) with normal lipids matched for age, race, and gender. After 3 consecutive weekly screening visits to ensure eligibility, including BP consistently within the defined ranges, subjects were referred to a nutritionist for instructions on the study diets.

**Diet**
A registered dietitian (K.L.M.) instructed each subject on how to plan and prepare these diets for home consumption. Each volunteer received written meal plans, recipe lists, and portion control information to match dietary goals. Subjects and investigators could not be blinded to obvious differences in the 2 diets. The diets were designed to maintain consistent intake of sodium, caffeine, and alcohol, which could influence BP. Each subject’s isocaloric energy intake was estimated by using the Harris Benedict equation, and calories were adjusted according to clinic weights to minimize weight changes. Subjects were monitored by the dietitian at least every 2 weeks to review their diet.

Subjects received a disposable camera to photograph all foods and beverages, and they also kept a food diary for 3 days, which included 2 working days and 1 nonworking day, before each study. These tools were used in combination, because the accuracy of self-reports is limited. Analysis of the diaries and photographs was conducted with Nutritionist Five software (First DataBank).

Physiological data, BP, and heart rate were measured in triplicate with subjects in the sitting position for the 3 qualifying visits and weekly thereafter for the remainder of the study. BP was measured by a trained observer using a mercury sphygmomanometer and appropriately sized cuff. Systolic BP was defined by the first Korotkoff sound, diastolic BP by the disappearance of the last (fifth) Korotkoff sound. Heart rate was measured by palpating the radial pulse for 60 seconds between the second and third BP measurement, with subjects seated.

**Hemodynamic Measurements**
The H.D.I.PulseWave CR-2000 was used to noninvasively assess BP, heart rate, systemic vascular resistance, stroke volume, cardiac output, large artery elasticity index, small artery elasticity index, and total vascular impedance. In brief, a tonometer was placed securely over the left radial artery for pulse waveform analysis, and a properly sized cuff was placed on the right upper extremity for BP measurements.

**Metabolic Data and Assay Methods**
The homeostatic model assessment of insulin resistance (HOMAIR) index was obtained as an index of insulin action. Plasma insulin was measured by radioimmunoassay (RIA).

**Nonesterified Fatty Acids and Lipids**
Blood for nonesterified fatty acids (NEFAs) was drawn into prechilled Eppendorf tubes containing para-oxon. Plasma was stored at −70°C before analyzing the total plasma NEFAs by using the 4Ni method. Triglycerides were measured by the fluorometric method. Total cholesterol was measured by the colorimetric method, and HDL-cholesterol was prepared from whole plasma by precipitation with phosphotungstate-MgCl₂. LDL and VLDL cholesterol were calculated.

**Ferric Reducing/Antioxidant Power of Plasma Assay**
Total antioxidant capacity was measured by the ferric reducing/antioxidant power of plasma (FRAP) assay under fasting conditions, with volunteers on their usual diet, and after 4 weeks each on the DASH-CD and low-antioxidant diets. The FRAP assay was performed in triplicate on each sample, and the mean of the 3 values was used in the analysis.

Plasma F₂-isoprostanes, a biomarker of oxidative stress, were measured on all 3 dietary phases by using gas chromatography/negative ion chemical ionization (GC/NICI) mass spectrometry as previously described.

**Study Design and Protocol**
After baseline studies on their usual diets, subjects entered an open-label randomized crossover study from the DASH-CD, which is high in antioxidants, to a low-antioxidant diet, which is comparable to the usual diet in most subjects, for 4 weeks each. On each of the 3 diets, subjects were admitted to the outpatient GCRC at 8:00 AM after an overnight fast. Intravenous access was established in both arms, with 1 side for obtaining blood samples and the other for infusion of intralipid and heparin. Baseline hemodynamic data were obtained at 5-minute intervals for 30 minutes. At the end of 30 minutes, blood samples were drawn for serum lipids and plasma insulin, total antioxidant capacity (FRAP), F₂-isoprostanes, NEFAs, and nitrite-nitrate. An infusion was then started of 20% intralipid (Baxter Healthcare Corp) at 0.8 mL · m⁻² · min⁻¹ and heparin (200-U bolus, followed by infusion at 1000 U/h). Heparin was given to activate lipoprotein lipase and accelerate the hydrolysis of fatty acids from triglycerides. Hemodynamic measurements were made, and blood samples were obtained for triglycerides, NEFAs, F₂-isoprostanes, and nitrite-nitrate at 2 hours and 4 hours of the intralipid and heparin infusion.

**Statistical Analysis**
Group comparisons for descriptive dichotomous variables, eg, gender, were made by using the χ² test. For descriptive numeric variables such as age, body mass index, nutrient intake, casual BP, and heart rate, the Student unpaired t test was used for between-group comparisons. Changes in hemodynamic variables, plasma total antioxidant capacity (FRAP), plasma F₂-isoprostanes, plasma nitrite-nitrate, and measures of insulin sensitivity were assessed by 2N S

Table 1. Selected Demographic and Biochemical Data in Obese and Lean Volunteers

<table>
<thead>
<tr>
<th>Variables</th>
<th>Obese Hypertensives (n=12)</th>
<th>Lean Normotensives (n=12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>35±2</td>
<td>39±2</td>
<td>NS</td>
</tr>
<tr>
<td>Gender, f/m</td>
<td>6/6</td>
<td>6/6</td>
<td>NS</td>
</tr>
<tr>
<td>Race, black/white</td>
<td>7/5</td>
<td>6/6</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>130±1</td>
<td>111±2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>92±1</td>
<td>72±2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>34.1±1.9</td>
<td>22.7±0.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td>229±6</td>
<td>173±7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL</td>
<td>47±3</td>
<td>61±5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LDL</td>
<td>152±5</td>
<td>95±6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>90±3</td>
<td>83±3</td>
<td>0.08</td>
</tr>
<tr>
<td>Urea nitrogen, mg/dL</td>
<td>3.4±0.15</td>
<td>4.32±0.08</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.90±0.05</td>
<td>0.92±0.03</td>
<td>NS</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>9.4±0.1</td>
<td>9.3±0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>3.4±0.1</td>
<td>3.5±0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.34±0.15</td>
<td>4.32±0.08</td>
<td>NS</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>5.5±0.3</td>
<td>4.5±0.3</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Data presented as mean±SEM.
using the general linear model for repeated measures. The Pearson correlation was used to assess the relationship of antioxidant capacity to BP. All statistical analyses were performed with the SPSS/PC 10.0 statistical software package (SPSS). A probability value <0.05 was accepted as statistically significant.

Results

Demographic and Biochemical Data

Demographic and biochemical data for the 12 lean normotensives and 12 obese hypertensives are shown in Table 1. Both groups had similar values for age, gender, and race. Obese hypertensives had higher values for total and LDL cholesterol, triglycerides, and uric acid and lower values for HDL cholesterol than did lean normotensives.

Nutritional Content of the Diets

The nutrient goals and average daily intakes for the usual diet, DASH-CD, and low-antioxidant diets estimated from food diaries and photographs are provided in Table 2. Caffeine intake was similar on the DASH-CD and low-antioxidant diets (43±7 versus 55±7 mg/d, P=NS). Although expected differences between the DASH-CD and the low-antioxidant diet were found, actual intakes for the DASH-CD deviated by 32% to 49% from goal for percentage of calories as saturated fat, cholesterol, dietary fiber, K⁺, Ca²⁺, Mg²⁺, vitamins C and A, and vegetables. The greatest discrepancy between expected and actual intake was present for low-fat dairy products. Actual intake for the low-antioxidant diet deviated from goal by 31% to 48% for cholesterol, dietary fiber, Ca²⁺, and vitamins C and A.

In comparing nutrient intake between obese and lean subjects on their usual diets, obese subjects had significantly lower caffeine intakes (30±6 mg/d) than did lean volunteers (79±12 mg/d, P<0.01). None of the other variables listed in Table 2 showed significant differences between the 2 groups on the usual diets. On the DASH-CD, obese subjects had significantly lower values than did lean volunteers for dietary K⁺ (2415±224 versus 3327±231 mg/d), vitamin C (253±32 versus 337±25 mg/d), and fruits (3.0±0.5 versus 4.6±0.6 exchanges/d). No significant differences between the 2 groups were observed for the other variables listed in Table 2.

On the low-antioxidant diet, a lower dietary fiber intake in lean volunteers than in obese volunteers (13.3±1.4 versus 9.7±0.9 g/d, P<0.05) was the only significant difference between the 2 groups. The lipid profiles within each group did not differ among the 3 dietary periods (Table 3).

Twenty-four–Hour Urinary Electrolytes

The mean of the 4 weekly values for 24-hour urinary Na⁺ for subjects on their usual diet, DASH-CD, and the low-antioxidant diets were not statistically different at 156±11, 138±14, and 158±16 mmol/d, respectively. Moreover, values for 24-hour urinary Na⁺ did not differ between lean and obese subjects on the different diets (usual, 156±18 versus 157±13 mEq/d; DASH-CD, 155±21 versus 141±20 mEq/d; low antioxidant, 158±27 versus 158±19 mmol/d; respectively). The mean of 4 weekly values for 24-hour urinary K⁺ were higher (P<0.05) in subjects on the DASH-CD (54±5 mmol/d) compared with the low-antioxidant diet (39±3 mmol/d) weekly. Twenty-four–hour urinary Ca²⁺ and
Mg$^{2+}$ values did not differ between the usual, DASH-CD, and low-antioxidant diets.

**Insulin Sensitivity**

Baseline values derived from the homeostatic model assessment of insulin resistance (HOMA IR) were greater in obese volunteers than in lean volunteers (Table 3).

Antioxidant capacity, as measured by FRAP, was greater in lean subjects than in obese subjects on normal diets. FRAP increased in obese volunteers but not in lean volunteers after 4 weeks on the DASH-CD (Table 3), and the group difference disappeared.

**BP Responses to the Dietary Interventions**

Systolic, diastolic, and mean BP declined significantly in obese hypertensives after weeks 3 and 4 on the DASH-CD compared with values on the baseline and low-antioxidant diets (Figure 1a through 1c). After 4 weeks on the DASH-CD, baseline BP in obese hypertensives was 18.1±1.5/7.4±1.6 mm Hg lower than on the low-antioxidant diet. Plasma antioxidant activity also correlated negatively with systolic BP in obese hypertensives after 4 weeks on the DASH-CD (r=–0.60, P<0.05). In obese hypertensives, the differences in systolic and diastolic BP on the usual and low-antioxidant diets were not significant (0.6±1.3/–0.6±1.3 mm Hg).

In lean normotensives, systolic BP tended to rise during weeks 2 and 3 of the low-antioxidant diet, but the difference compared with that of the DASH-CD was not significant. Diastolic and mean BPs were higher (P<0.05) after 3 weeks on the low-antioxidant diet than on the DASH-CD (Figure 1b and 1c), but the difference between the 2 diets was not significant at 4 weeks.

Mean values for heart rate in obese subjects were 5 bpm greater after 4 weeks on the low-antioxidant diet than on the DASH-CD, but the difference was not statistically significant (P=0.15). Heart rate did not differ between the various dietary phases in lean normotensives.

### Acute Hyperlipidemia

The intralipid and heparin infusion increased plasma triglycerides and NEFAs after 2 and 4 hours on all 3 diets in both lean normotensives and obese hypertensives (Figures 2a and 2b). The changes in plasma triglycerides during intralipid and heparin infusion were similar within and between both groups on all 3 diets. NEFAs tended to increase more in lean volunteers than in obese volunteers during the infusion of intralipid and heparin.

After 4 hours of the intralipid and heparin infusion, systolic BP increased significantly in obese hypertensives and in lean normotensives on all 3 diets. Despite the increase with acute hyperlipidemia, systolic and diastolic BP in obese hypertensives remained lower on the DASH-CD than on the usual and low-antioxidant diets (Figures 3a and 3b).

Small artery elasticity index decreased in lean normotensives and in obese hypertensives during the intralipid and heparin infusion when they were on usual and low-antioxidant diets. However, small artery elasticity did not decline during the infusion of intralipid and heparin in obese subjects on the DASH-CD (Figure 3c), as it did in lean normotensives.

### F$_2$-Isoprostanes

Plasma F$_2$-isoprostanes increased in both groups during the 4-hour infusion of intralipid and heparin when subjects were consuming their usual and low-antioxidant diets (Figure 2c). However, plasma F$_2$-isoprostanes did not increase significantly in obese hypertensives during intralipid and heparin after 4 weeks on the DASH-CD.

### Discussion

In this study, obese subjects with BP values in the high-normal–to–stage 1 hypertension range (hypertensives) and evidence for the metabolic syndrome had a significant decline in BP (–8.1±1.5/7.4±1.6 mm Hg) when they followed a DASH-CD prescription over 4 weeks (Figure 1). In contrast,

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**TABLE 3. Data on Weight and Markers of Insulin Resistance and Antioxidant Capacity Shown Separately for Obese Hypertensives and Lean Normotensives on the 3 Diets**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Obese Hypertensives (n=12)</th>
<th>Lean Normotensives (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Usual Diet</td>
<td>DASH-CD</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>101±6</td>
<td>100±6</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td>209±8</td>
<td>206±8</td>
</tr>
<tr>
<td>HDL</td>
<td>44±3</td>
<td>42±3</td>
</tr>
<tr>
<td>LDL</td>
<td>131±8</td>
<td>125±8</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>168±29</td>
<td>191±42</td>
</tr>
<tr>
<td>Insulin, μU/mL</td>
<td>12.5±1.1</td>
<td>15.1±2.3</td>
</tr>
<tr>
<td>HOMA IR</td>
<td>51±15</td>
<td>63±18</td>
</tr>
<tr>
<td>FRAP, μmol/L</td>
<td>271±15</td>
<td>334±27*</td>
</tr>
<tr>
<td>F$_2$-Isoprostanes</td>
<td>42±5</td>
<td>40±5</td>
</tr>
</tbody>
</table>

Values are mean±SEM. HOMA IR indicates homeostatic model assessment of insulin resistance; FRAP, ferric reducing activity of plasma.

* P<0.05 vs baseline; †P<0.05 lean vs obese.
BP did not change significantly in lean normotensives after 4 weeks on the DASH-CD. Although systolic BP was \( \approx 5 \) mm Hg higher during the second and third weeks of the low-antioxidant diet than of the DASH-CD in lean normotensives, the difference was not significant.

The decrease of systolic BP in obese hypertensives is similar in magnitude to that seen in hypertensive patients with the high fruits-and-vegetables component of DASH diet and less than that seen among hypertensive patients in the original DASH-CD. The more limited effect of our DASH-CD prescription on BP compared with the sentinel study may reflect the incomplete dietary adherence of our volunteers (Table 2). The failure of BP to decline significantly in lean volunteers on the DASH-CD did not reflect poorer dietary adherence than that of obese subjects, as noted in the Results. In fact, if anything, the lean normotensives had better dietary adherence, as evidenced by greater consumption of fruit and estimated daily \( K^+ \) intake compared that of with the obese hypertensives on their usual diets (Table 2).

The explanation for the discrepancies in goal versus actual dietary intake was probably a function of study design. Subjects were instructed to plan and prepare their own meals. By comparison, in the original DASH study, subjects received prepackaged meals. Second, many subjects were reluctant to increase low-fat dairy products to the target level. Although attempts were made to encourage consumption of \( Ca^{2+} \)-fortified foods, actual \( Ca^{2+} \) intake was \( \approx 60\% \) of goal. Despite limited adherence, subjects consumed a statistically higher intake of total fruits, vegetables, and low-fat dairy products on DASH-CD than on the low-antioxidant diet.

The DASH-CD may lower BP by raising antioxidant capacity and improving the balance between antioxidant defenses and oxidative stress. Antioxidant capacity, measured by the FRAP assay, was higher in lean normotensives than in obese hypertensives on their usual diets (Table 3). After 4 weeks on the DASH-CD, plasma antioxidant capacity increased significantly in obese hypertensives but not in lean normotensives, and the group difference was eliminated. Although \( F_2 \)-isoprostanes, a marker of oxidative stress, did not change with diet, oxidative stress may raise BP and has emerged as a possible mechanism by which obesity and insulin resistance raise BP. Moreover, oxidative stress is a common signal transduction mechanism by which various risk factors may induce vascular remodeling.

The DASH-CD is high in antioxidants contained in fruits, vegetables, and whole grains, and this diet raised antioxidant capacity (Table 3) compared with that of usual diets in the...
obese volunteers. In the present study, we do not have evidence that the DASH-CD reduced oxidative stress under basal conditions using F₂-isoprostanes as a biomarker. There are multiple biomarkers of oxidative stress in vivo, which have various advantages and limitations. Among the more notable limitations is the lack of tissue and signal transduction pathway specificity, particularly in target tissues critical in BP regulation. It is not clear in this study whether oxidative stress did not change on the DASH-CD or if plasma F₂-isoprostanes did not reflect a true change. Based on the data, the benefits of the DASH-CD on BP may be mediated in part by improving the balance between antioxidant capacity and oxidative stress in obese subjects.

The difference in total antioxidant capacity between obese hypertensives and lean normotensives on their usual diets was noted previously. Tse et al documented that hypertensive patients had lower levels of ascorbic acid and albumin-corrected thiol levels, than those of normotensive volunteers. In another study, plasma ascorbic acid was inversely related to systolic and diastolic BP of hypertensive patients independently of other traditional factors, and changes of ascorbic acid with nutritional depletion and repletion preceded changes of BP. In the present study, vitamin C consumption was ≈3 times greater in both lean and obese subjects on the DASH-CD than on the usual diet. Vitamin C decreases NADPH oxidase, a major superoxide-generating enzyme, in spontaneously hypertensive rats. These data suggest that increasing antioxidant capacity can reduce the genesis of reactive oxygen.

Our results indicate that borderline and stage 1 hypertensive, obese, dyslipidemic subjects have a lower total antioxidant capacity than that of lean normotensive volunteers with normal lipids, when both groups are consuming their usual diets. These data raise the possibility of an imbalance between the production of reactive oxygen species and the capacity of antioxidant defenses in obese subjects, which could contribute to elevated BP. The DASH-CD may improve this imbalance in obese hypertensive patients.

Obesity is associated with hypertension and insulin resistance. Weight loss lowers BP and reduces insulin resistance in obese hypertensive subjects. Insulin resistance is also a risk factor for cardiovascular disease, and markers of insulin resistance are associated with hypertension. Thus, effects of the DASH-CD on weight and insulin resistance could account for some of the BP reduction observed in obese hypertensives. However, weight did not change significantly throughout the study in either group. Although evidence for insulin resistance was more apparent...
in obese volunteers than in lean volunteers (Table 3), these indices were not significantly different within either group among the 3 diets. From the available data, the BP decline in obese hypertensives on the DASH-CD was probably not explained by changes of weight or insulin sensitivity.

Components of the DASH-CD in addition to antioxidants may contribute to the BP decline. Based on food records, the DASH-CD contained more K⁺, Ca²⁺, and Mg²⁺ and less Na⁺ than did the usual and low-antioxidant diets, and 24-hour urine K⁺ values were also greater on the DASH-CD than on the low-antioxidant diet. Although 24-hour urine Na⁺ tended to be lower on the DASH-CD than the other dietary periods, the differences were not significant. Although the differences in cation consumption may have contributed to the BP decline in obese hypertensives on the DASH-CD, previous studies suggest that the magnitude of changes achieved is modest and insufficient to explain the BP reduction observed.³⁷,³⁸ To further complicate efforts to separate the effect of dietary minerals and antioxidant on BP, K⁺ and Mg²⁺ have antioxidant effects.³⁹,⁴⁰

We reported that an infusion of intralipid and heparin raises BP and increases oxidative stress as measured by F₂-isoprostanes in lean normotensives and obese hypertensives.¹¹,¹² In the present study, lean normotensive and obese hypertensive subjects following usual, DASH-CD, and low-antioxidant diets also had an increase in systolic BP during an intralipid and heparin infusion. Similar to our previous study, intralipid and heparin increased plasma F₂-isoprostanes in lean normotensives and in obese, dyslipidemic, hypertensive subjects on their normal diets, as well as during the low-antioxidant diet. In contrast, F₂-isoprostanes did not increase significantly during acute hyperlipidemia when obese subjects were consuming the DASH-CD. One implication of these findings is that the DASH-CD enhances antioxidant capacity, which, in turn, attenuates the oxidative stress response induced by acute hyperlipidemia.

Although oxidative stress, as measured by F₂-isoprostanes, did not increase during the infusion of intralipid and heparin among obese subjects consuming a DASH-CD, their BP rose similarly during acute hyperlipidemia on all 3 diets (Figure 2). These observations suggest that BP and oxidative stress, as measured by F₂-isoprostanes, are not linked in the setting of acute hyperlipidemia. However, small-artery distensibility, a measure of endothelial function,⁴¹ did not fall during acute hyperlipidemia in obese hypertensives on DASH-CD, as it did on the other 2 diets (Figure 3). Thus, the antioxidant actions of the DASH-CD may have important vasculoprotec-
tive effects, which could contribute to BP benefits over the longer-term.

In conclusion, the DASH-CD emerges as a clinically useful tool in the outpatient management of free-living obese subjects with high-normal and stage 1 hypertension, as well as other evidence for the cardiovascular risk factor cluster. Even though dietary adherence is imperfect, acute lipid-induced oxidative stress and impairment of small-artery distensibility are blunted in obese hypertensives following a DASH-CD. Moreover, after 4 weeks on the DASH-CD, antioxidant capacity rises and BP falls in obese hypertensives but not in lean normotensives. These findings suggest that the DASH-CD lowers BP in obese hypertensive patients by improving the balance between antioxidant capacity and oxidative stress.

**Perspective**

A diverse and expanding literature implicates excessive oxidative stress and/or inadequate antioxidant defenses in the pathogenesis of cardiovascular risk and disease. Given the epidemic status of the metabolic syndrome, which is driven principally by unhealthy lifestyle patterns, this topic is assuming progressively greater importance. Unfortunately, achieving healthy lifestyle patterns can be challenging. Therefore, it would seem useful to define the minimum intervention required to elicit clinically relevant risk reduction. The present study indicates that the DASH-CD prescription in obese free-living individuals with evidence for the metabolic syndrome, despite suboptimal adherence, results in clinically important improvements of BP. Further studies to separate the effects of various foods from their mineral and antioxidant content may help establish whether dietary changes are required or if supplements are adequate to achieve substantial risk reduction.

**Acknowledgments**

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