Abstract—In 16 African Americans (blacks, 14 men, 2 women) with average admission mean arterial pressure (MAP, mm Hg) 99.9 ± 3.5 (mean ± SEM), we investigated whether NaCl-induced renal vasoconstriction attends salt sensitivity and, if so, whether supplemental KHCO₃ ameliorates both conditions. Throughout a 3-week period under controlled metabolic conditions, all subjects ate diets containing 15 mmol NaCl and 30 mmol potassium (K⁺) (per 70 kg body wt [BW] per day). Throughout weeks 2 and 3, NaCl was loaded to 250 mmol/d; throughout week 3, dietary K⁺ was supplemented to 170 mmol/d (KHCO₃). On the last day of each study week, we measured renal blood flow (RBF) and glomerular filtration rate (GFR) using renal clearances of PAH and inulin. Ten subjects were salt sensitive (SS) (ΔMAP > +5%) and 6 salt resistant (SR). In NaCl-loaded SS but not SR subjects, RBF (mL/min/1.73 m²) decreased from 920 ± 75 to 828 ± 46 (P < 0.05); filtration fraction (FF, %) increased from 19.4 ± 21.4 (P < 0.001); and renal vascular resistance (RVR) (10² × mm Hg/[mL/min]) increased from 101 ± 8 to 131 ± 10 (P < 0.001). In all subjects combined, ΔMAP varied inversely with ΔRBF (r = −0.57, P = 0.02) and directly with ΔRVR (r = 0.65, P = 0.006) and ΔFF (r = 0.59, P = 0.03), but not with MAP before NaCl loading. When supplemental KHCO₃ abolished the pressor effect of NaCl in SS subjects, RBF was unaffected but GFR and FF decreased. The results show that in marginally K⁺-deficient blacks (1) NaCl-induced renal vasoconstrictive dysfunction attends salt sensitivity; (2) the dysfunction varies in extent directly with the NaCl-induced increase in blood pressure (BP); and (3) is complexly affected by supplemented KHCO₃, GFR and FF decreasing but RBF not changing. In blacks, NaCl-induced renal vasoconstriction may be a pathogenetic event in salt sensitivity. (Hypertension. 1999;33:633-639.)

Key Words: race ■ normotension ■ kidney ■ sodium chloride, dietary ■ potassium

Blood pressure (BP) can be judged to be salt sensitive (SS) when it varies directly and substantially with the dietary intake of NaCl. Given that the occurrence of normotensive salt sensitivity increases the likelihood of later hypertension, the same mechanism may mediate salt sensitivity in both conditions and that mechanism may be critical to the pathogenesis of SS hypertension. In patients with essential hypertension, the mechanism of salt sensitivity may involve a dysfunctional renal hemodynamic response to increased dietary NaCl: With NaCl loading, renal blood flow (RBF) may either fail to increase⁶–⁹ or may decrease¹⁰,¹¹ such that both renal vascular resistance (RVR)⁶–¹¹ and filtration fraction (FF)⁷,⁹,¹¹ increase, with glomerular filtration rate (GFR) persisting unchanged¹⁰,¹¹ or increasing.⁷,¹²,¹³ In African Americans (blacks) with SS hypertension, administration of nifedipine that corrected an NaCl-induced increase in BP also corrected an attending NaCl-induced reduction in RBF and the consequent increase in FF.¹⁰ If such an NaCl-induced renal vasoconstrictive dysfunction is a critical mediator of salt sensitivity in many hypertensive blacks, and normotensive and hypertensive salt sensitivity in many cases reflects different stages of the same disorder, NaCl-induced renal vasoconstrictive dysfunction may be a critical mediator of salt sensitivity in many blacks regardless of their basal level of BP. This possibility seems not to have been investigated.

When dietary potassium (K⁺) was controlled at a marginally deficient intake of 30 mmol/d, not uncommon in many blacks, we recently observed that salt sensitivity occurred in the great majority of normotensive blacks but in relatively few normotensive whites and on average was more severe in blacks. In both, increasing dietary K⁺ attenuated salt sensitivity. In the current study of black men and women in whom the values of BP before dietary intervention ranged from normal to mildly increased and in whom dietary intake of K⁺ was initially set at a marginally deficient intake, we asked these questions: (1) In those who are SS, does dietary salt loading induce a renal vasoconstrictive dysfunction? (2) If so, does its severity vary either with the level of BP before NaCl

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loading or the NaCl-induced increase in BP? (3) Is the dysfunction affected by supplemental dietary K\(^+\) that abolishes salt sensitivity?

### Methods

#### Participants

Participants were recruited through advertisement/flyers and through word-of-mouth referral. Selection criteria included self-identification as black, age ≥25 and ≤60 years, body weight (BW) within 30\% of ideal, no history of acute or chronic diseases, in particular renal disease, ischemic heart disease, stroke, or diabetes, and no regular medication. Participants were admitted to the General Clinical Research Center (GCRC) at the University of California at San Francisco (UCSF) for 21 days. The study was approved by and conducted according to the guidelines of the Committee on Human Research at UCSF. Participants gave written informed consent.

#### Diets

Throughout the study, participants ate a diet that provided an amount of energy calculated to keep their BW constant, with total calories derived from protein \(10\%\), carbohydrates \(45\%\), and fat \(45\%\). Per 70 kg of BW, the basal diet provided 15 mmol Na\(^+\), 30 mmol K\(^+\), and 14 mmol Ca\(^2+\). Ingredients for all meals, preparation of meals, and the time of meal provision were kept constant throughout the study. Participants received 25 to 30 g/kg BW/d of deionized water during the low NaCl phase and 40 g/kg BW/d during the high NaCl phase, respectively.

#### BP and BW

We measured BP every 4 hours after 15 minutes of rest in the supine position using an automated oscillometric device (Dinamap, Critikon Inc) programmed to obtain 5 readings within 5 minutes, and average daily pressures were calculated. BW was measured daily at 6 AM before breakfast. Average BPs and BWs of the last 2 days of each study period before renal hemodynamic measurements are reported.

#### Renal Hemodynamics

On the last day of each study period, 2 hours after breakfast and after an oral water load of 1 L administered over an hour, participants received an intravenous bolus of 5% inulin and 5% PAH dissolved in 5% glucose, followed by inulin and PAH continuous infusions. Doses were calculated to achieve steady-state inulin and PAH plasma concentrations of 15 to 20 mg/L and 1.5 to 2 mg/L, respectively. Deionized water was administered orally at 200 to 250 mL/20 min throughout the renal hemodynamics measurements. Participants remained in supine position except for urination, during which they stood up for 1 to 2 minutes. After a 1-hour equilibration period, three 20-minute timed urine samples and midtime blood samples were obtained. BP was measured at 5-minute intervals.

#### Laboratory Measurements

Spontaneously voided urine was collected daily over 24-hour periods except on the day of renal hemodynamics measurements. PAH, inulin, and electrolyte concentrations and hematocrits were determined in blood and urine samples at the GCRC Core Laboratory by use of standard techniques.

### Results

As judged by an increase in MAP of >5\% on high (250 mmol/d) compared with low (15 mmol/d) NaCl intake, 10 (9 men, 1 woman) of 16 participants were classified as SS and 6 (5 men, 1 woman) as salt resistant (SR). \(\Delta MAP\%\) 13.2 ± 1.8 versus 2.5 ± 0.9, respectively, \(P<0.001\). Baseline characteristics (Table 1) were not different between the 2 groups although SR subjects tended to be heavier. Three of 10 SS and 2 of 6 SR subjects were mildly hypertensive on admission. Throughout the course of the study, urine volumes, daily and cumulative urinary Na\(^+\) and K\(^+\) excretion, Na\(^+\) balance, and serum electrolytes were not different between groups except that serum Cl\(^-\) increased with NaCl loading in SS subjects and serum K\(^+\) was slightly but significantly lower in SR subjects at the end of LL. K\(^+\) repletion with KHCO\(_3\) increased serum K\(^+\) levels significantly in both groups (Table 2).

### Data Analysis

Effective renal plasma flow (ERPF), RBF, and GFR were calculated from urine and plasma PAH and inulin concentrations and hematocrit values. We calculated FF by GFR/ERPF × 10\(^3\) (using MAP measured during renal hemodynamics studies). Intrarenal resistances and glomerular capillary pressure were estimated for the LL and HL periods by use of the renal function curves. The effect of diets on 24-hour BP, BW, electrolytes, and renal hemodynamic parameters was assessed by repeated measure ANOVA and contrast analysis. Differences between groups at baseline and differences in diet-induced changes were analyzed by unpaired and paired \(t\) test, respectively. Stepwise linear regression analysis was performed to assess the effect of independent variables on renal hemodynamics. Data are expressed as mean ± SEM. The null hypothesis was rejected at \(P<0.05\).

### Effect of NaCl Loading on BP, Renal Hemodynamics, BW, and Electrolytes

In SS versus SR subjects, respectively, NaCl loading increased systolic BP (SBP) (mm Hg) 17.3 ± 1.7 versus 5.5 ± 1.9, \(P<0.001\); diastolic BP (DBP) (mm Hg) 9.7 ± 1.8 versus 0.8 ± 1.0, \(P<0.01\); and MAP (mm Hg) 12.2 ± 1.9 versus 2.3 ± 0.9, \(P<0.001\) (Figure 1A). Only in SS subjects did NaCl loading increase DBP and MAP significantly. With NaCl loading, BW (kilograms) increased (2.4 ± 0.2 versus 2.8 ± 0.6) and hematocrit decreased (−0.037 ± 0.005 versus −0.039 ± 0.01) significantly and to a similar degree in both groups (Table 2). In SS versus SR subjects, NaCl

### Table 1. Baseline Data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Salt Sensitives</th>
<th>Salt Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Age, y</td>
<td>43±2</td>
<td>47±3</td>
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<tr>
<td>SBP, mm Hg</td>
<td>136±5</td>
<td>138±11</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>84±2</td>
<td>77±8</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>101±3</td>
<td>97±9</td>
</tr>
<tr>
<td>BW, kg</td>
<td>77±4</td>
<td>84±7</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>24±1</td>
<td>27±2</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>97±6</td>
<td>88±4</td>
</tr>
</tbody>
</table>

Values are mean ± SEM. \(P=NS\).
TABLE 2. Effect of NaCl Loading and Potassium Supplementation on Blood Pressure, Body Weight, and Serum and Urine Electrolytes in Salt-Sensitive and Salt-Resistant African Americans

<table>
<thead>
<tr>
<th>Variables</th>
<th>Salt-Sensitive Subjects</th>
<th>Salt-Resistant Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diet LL</td>
<td>LL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>125±4</td>
<td>143±5*</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>76±2</td>
<td>86±2*</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>93±2.5</td>
<td>105±3*</td>
</tr>
<tr>
<td>BW, kg</td>
<td>72.4±3.5†</td>
<td>74.8±3.5*</td>
</tr>
<tr>
<td>Serum Na, mmol/L</td>
<td>137±1</td>
<td>141±0*</td>
</tr>
<tr>
<td>Serum K, mmol/L</td>
<td>3.68±0.05†</td>
<td>3.36±0.05</td>
</tr>
<tr>
<td>Cum Na intake, mmol/wk</td>
<td>110±4</td>
<td>127±3*</td>
</tr>
<tr>
<td>Cum K intake, mmol/wk</td>
<td>167±8</td>
<td>209±6*</td>
</tr>
<tr>
<td>Cum UNaV, mmol/wk</td>
<td>226±30†</td>
<td>1097±97*</td>
</tr>
<tr>
<td>Cum UCr, mmol/wk</td>
<td>141±10†</td>
<td>195±16*</td>
</tr>
</tbody>
</table>

Values are mean±SEM. LL indicates Na⁺ and K⁺ intakes (mmol/70 kg per day) of 15 and 30, HL and 250 and 30, and HH of 250 and 170, respectively. UNaV, UCr indicates urinary excretion rates of sodium and potassium, respectively; FeNa, fractional excretion of sodium. BPs, BW, UNaV, UCr, and percent FeNa were determined for each subject as the average of the last 2 days of each study period. Serum electrolytes and hematocrit were measured on the last day of each study period. Serum HCO₃⁻ was measured in arterialized venous blood samples. Cum Na intake, Cum K intake, Cum UNaV, Cum UCr are weekly cumulative Na and K intakes and excretion rates, respectively. Values for sodium and potassium intake and all urine values are weight-corrected to 70 kg of BW. FeNa was calculated from (UNa/Serum Na)/(UCr/Serum Cr) and excretion rates, respectively. Values for sodium and potassium intake and all urine values are weight-corrected to 70 kg of BW. FeNa was calculated from (UNa/Serum Na)/(UCr/Serum Cr)×100.

*P<0.01, LL vs HL; †P<0.01, LL vs HH; ‡P<0.01, HL vs HH; §P<0.05, LL vs HH; ||P<0.05, HL vs HH. P values are by ANOVA.

loading had opposite effects on RBF (mL/min/1.73 m²) (−93±35 versus 50±47, P<0.05) (Figure 1B), FF (%) (2.0±0.6 versus −1.4±0.8, P<0.01) (Figure 1C), RVR (10¹×mm Hg/[mL/min]) (29±7 versus −3±6, P<0.01) (Figure 1D), afferent renal arteriolar resistance (Ra), efferent renal arteriolar resistance (Re), and glomerular capillary pressure (Pgc) (Table 4), respectively. NaCl loading (HL) compared with low NaCl (LL) induced

Figure 1. Changes in MAP (A), RBF (B), FF (C), and RVR (D) induced by increasing dietary salt intake from 15 to 250 mmol/d in SS vs SR blacks. Values are mean±SEM. *P<0.05 compared with low salt intake.
significant changes in RBF, FF, RVR, Ra, Re, and PGCS in SS subjects only (Tables 3 and 4). GFR did not change significantly with NaCl loading in either group but trended upward in SS subjects.

When the renal effects of NaCl loading were analyzed separately in those 7 SS subjects with baseline BPs in the normal range, results were not different from those of all SS subjects combined (ΔRBF [HL-LL] = 104±35 mL/min/1.73 m², P<0.01; ΔGFR 6±6 mL/min/1.73 m², P=NS; ΔFF 2.6±0.7%, P<0.01; ΔRVR 34±8 mm Hg/[mL/min], P<0.01) (Figure 2).

In all subjects combined, stepwise linear regression analysis revealed that the NaCl-induced change in MAP strongly predicts the changes in RBF, FF, and RVR (Figure 3) but not GFR. Age, MAP before NaCl loading, and Na⁺ balance were not predictive of NaCl-induced changes in renal hemodynamics. The severity of salt sensitivity was not related to the BP change before NaCl loading (MAP during LL versus ΔMAP [HL-LL]; r=0.134, P=NS).

**Effect of K⁺ Supplementation on BP, Renal Hemodynamics, BW, and Electrolytes**

In SS subjects, dietary K⁺ supplementation abolished the NaCl-induced increases in BP. In SR subjects, K⁺ depletion decreased DBP and MAP but not SBP to a level significantly lower than that occurring during LL (Table 2). In SS subjects, SBP decreased by -18.5±2.4, in SR -11.0±4.7 mm Hg, P=NS; DBP -9.0±1.8 versus -5.7±2.0 mm Hg, P=NS; MAP -12.2±1.9 versus -7.5±2.9 mm Hg, P=NS. K⁺ supplementation reversed the NaCl-induced increases in RVR and FF observed in SS subjects but it did not change RBF (Table 3). GFR and FF decreased significantly with K⁺ supplementation in SS subjects. In SR subjects, K⁺ supplementation induced a small, not statistically significant decrease in GFR. Changes in renal hemodynamics were not predicted by the change in MAP induced by KHCO₃. Pressor and renal hemodynamic effects induced by KHCO₃ were not significantly different between SS and SR subjects with 1 exception: ΔFF = -2.8±0.5 in SS subjects versus 0.4±1 in SR subjects, P<0.01. With K⁺ supplementation, weekly cumulative Na⁺ excretion and changes in BW, hematocrit, serum Na⁺, Cl⁻ and K⁺ were similar in SS and SR subjects (Table 2).

**Discussion**

The results of this study show that in SS blacks with either normal or mildly elevated BP, NaCl loading induced a renal vasoconstrictive dysfunction in which RBF decreased, RVR and FF increased, and GFR trended upward. In those normotensive and hypertensive subjects who were not SS, renal dysfunction was not observed when NaCl was loaded. In all subjects combined, neither the extent of NaCl-induced increase in BP nor that of the NaCl-induced renal dysfunction was related to the level of BP measured immediately before NaCl loading. However, the increase in BP induced by NaCl loading varied directly with the extent of renal dysfunction so induced. Specifically, the changes in MAP induced by dietary

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**TABLE 3. Effects of Salt Loading and Potassium Supplementation on Renal Hemodynamics in Salt-Sensitive and Salt-Resistant African Americans**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Salt-Sensitive Subjects</th>
<th></th>
<th>Salt-Resistant Subjects</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LL</td>
<td>HL</td>
<td>HH</td>
<td>P</td>
</tr>
<tr>
<td>GFR, mL/min per 1.73 m²</td>
<td>102±4†</td>
<td>108±5</td>
<td>89±4‡</td>
<td>0.0003</td>
</tr>
<tr>
<td>RBF, mL/min per 1.73 m²</td>
<td>920±57†</td>
<td>828±46‡</td>
<td>830±67</td>
<td>0.02</td>
</tr>
<tr>
<td>ERPF, mL/min per 1.73 m²</td>
<td>540±34</td>
<td>521±30</td>
<td>498±37</td>
<td>NS</td>
</tr>
<tr>
<td>FF, %</td>
<td>19.4±0.9</td>
<td>21.4±1.1*</td>
<td>18.6±1.1‡</td>
<td>0.0003</td>
</tr>
<tr>
<td>RVR, 10³ mm Hg/(mL/min)</td>
<td>101±8†</td>
<td>131±10*</td>
<td>120±12</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Values are means±SEM. LL indicates Na⁺ and K⁺ intakes (mmol/70 kg per day) of 15 and 30, HL of 250 and 30, and HH of 250 and 170, respectively. During HH, K⁺ was supplemented as its bicarbonate salt.

*P<0.01; †P<0.01; ‡P<0.01, LL vs HH; §P<0.05, LL vs HL; ¶P<0.05, LL vs HH; ||P<0.05, HL vs HH. P values are by ANOVA.

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**TABLE 4. Effects of Salt Loading on Intrarenal Vascular Resistances and Glomerular Capillary Pressure in Salt-Sensitive and Salt-Resistant African Americans**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Salt-Sensitive Subjects</th>
<th></th>
<th>Salt-Resistant Subjects</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LL</td>
<td>HL</td>
<td>Δ</td>
<td>P†</td>
</tr>
<tr>
<td>Ra, 10³×mm Hg/(mL/min)</td>
<td>59.7±5.1</td>
<td>68.4±6</td>
<td>9.7±9</td>
<td>0.01</td>
</tr>
<tr>
<td>Re, 10³×mm Hg/(mL/min)</td>
<td>41.7±4.1</td>
<td>61.4±6.2</td>
<td>19.7±5.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Pgc, mm Hg</td>
<td>39.7±0.8</td>
<td>49.3±2.1</td>
<td>9.6±4.9</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are mean±SEM. LL indicates dietary Na⁺ and K⁺ intakes (mmol/70 kg per day) of 15 and 30, HL of 250 and 30, respectively. Δ indicates LL-HL.

*P<0.01 for salt-sensitive vs salt-resistant subjects.

†P=NS for LL vs HL by paired t test.
NaCl varied inversely with those induced in RBF and directly with those in RVR and FF.

A similar pressor-renal hemodynamic relationship with NaCl loading was observed by van Paassen et al\(^\text{21}\) in a group of predominantly white male patients selected only for hypertension. These investigators proposed that in hypertensive patients, “a rise in blood pressure in response to a high Na\(^+\) intake appears to partially be the result of insufficient renal vasodilation” and a consequent impaired capacity to excrete NaCl. Such a dysfunctional renal hemodynamic response to NaCl loading was earlier formulated by Hollenberg and Williams\(^\text{22}\) to mediate salt sensitivity in patients selected for “nonmodulating” essential hypertension. In support of these formulations, in both black and white patients with hypertension, pharmacological agents that ameliorated an NaCl-induced rise in BP also ameliorated an attending renal hemodynamic dysfunction.\(^\text{10,21,22}\) We propose that in normotensive as well as hypertensive blacks, NaCl-induced renal vasoconstrictive dysfunction can be a critical mediator of salt sensitivity. Since occurrence of normotensive salt sensitivity reportedly increases the likelihood that SS hypertension will occur within a decade,\(^\text{2,4,5}\) both conditions in blacks could reflect different stages of a single disorder in which NaCl-induced renal vasoconstriction is a critical pathogenetic component.

The NaCl-induced renal vasoconstrictive dysfunction currently observed in SS blacks is similar to that previously described in hypertensive black,\(^\text{10}\) white,\(^\text{11}\) and Japanese\(^\text{23}\) subjects selected for salt sensitivity. In these studies, however, as in those of SS patients with nonmodulating essential hypertension,\(^\text{22}\) the renal hemodynamic dysfunction that occurred with NaCl loading was not reported to vary in extent with that of the increase in BP induced by NaCl loading. Further, in these studies as in those of van Paassen et al,\(^\text{21}\) preexisting hypertension and “fixed vascular changes in the hypertensive kidney” may have been necessary pathogenetic components of both the NaCl-induced rise in BP and the attending renal hemodynamic dysfunction. By contrast, in

![Graphs A, B, C, D](http://hyper.ahajournals.org/)

**Figure 2.** MAP, RBF, FF, and RVR during low (LL) and high (HL) salt intake in 7 SS subjects with baseline BPs in the normotensive range. Values are mean±SEM.

![Graphs A, B, C, D](http://hyper.ahajournals.org/)

**Figure 3.** Relationship between salt-induced change in ΔMAP and changes in ΔRBF (A), ΔGFR (B), ΔFF (C), and ΔRVR (D).
most of the currently studied blacks with salt sensitivity, the NaCl-induced reduction in RBF occurred unassociated with hypertensive levels of BP and persisted after supplemental dietary K+ abolished the NaCl-induced increase in BP. Hence, the renal vasoconstriction induced by dietary NaCl did not depend on either the concomitance of hypertension or rise in BP (or a marginal dietary intake of K+) and, thus, could of itself have mediated salt sensitivity, ie, in the absence of “fixed vascular changes.” However, over time, such a renal vasoconstrictive dysfunction in blacks could contribute to the pathogenesis of renal disease expressed as SS hypertension (vide infra).

Although Na+ retention and volume expansion are considered critical events in the pathogenesis of SS hypertension,24 Na+ balance does not necessarily predict changes in BP responses in normotensive or in hypertensive subjects.10,25–28 In studies of the Dahl rat, NaCl loading increased plasma volume and cardiac output equally in SS rats (DS) and SR rats (DR), but total peripheral vascular resistance decreased only in DR.29 When volume expansion was prevented in NaCl-loaded DS, BP did not rise.29 The investigators concluded that in the DS, the plasma volume expansion induced by NaCl loading was necessary but not sufficient to induce hypertension. They proposed that an impaired cardiovascular response to that expansion was also necessary. In SS and SR subjects in the current study, NaCl loading induced a similarly positive Na+ balance and seemed to induce a similar expansion of plasma volume, as judged by the occurrence in both groups of similar decreases in hematocrit and increases in BW. This would suggest that plasma volume expansion is not sufficient to effect salt sensitivity. However, the fact that supplemental dietary K+ that abolished salt sensitivity also natriuretically contracted the apparently expanded plasma volume suggests that expansion was necessary for the expression of that salt sensitivity. The fact that the NaCl-induced reduction in RBF persisted unchanged when K+ supplementation abolished the NaCl-induced increase in BP shows that this NaCl-induced renal hemodynamic dysfunction is not of itself sufficient to mediate salt sensitivity. Thus, given the direct relationship between the increase in BP and the decrease in RBF observed with NaCl loading in the blacks currently studied, both this dysfunction and plasma volume expansion may have been necessary, yet possibly not sufficient, for the NaCl-induced pressor effect.

Like Guyton,30,31 most investigators assume that a sustained increase in BP induced by NaCl–salt sensitivity—is a consequence of an impaired capacity of the kidney to excrete salt at a lower BP, pressure natriuresis being required to overcome that impairment and to restore the capacity of the kidney to maintain NaCl and water balance. According to one formulation,32 hypertension becomes SS when either the renal ultrafiltration coefficient (Kf) is reduced or the renal tubular reabsorption of NaCl is increased or both. In both instances, an increased Poc is believed to occur and to mediate pressure natriuresis. An NaCl-induced increase in GFR has been reported in SS normotensive white men,33 in a racially mixed group of SS hypertensive subjects,7 and in black hypertensive subjects12 and is inferred to reflect an increase in Re that increases Poc, thereby facilitating pressure natriuresis, if over time causing renal damage in trade-off.10,11 As reported previously in SS hypertensive subjects,7,10,11 in the current study, NaCl loading induced in SS but not in SR blacks an increase in FF, Poc, and Re. In the current study, these increases varied directly with those in MAP.

In the current study, supplementing dietary K+ with KHCO3 not only abolished the NaCl-induced increase in BP and FF without affecting RBF but also induced a large decrease in GFR. The decrease in GFR may be in part a consequence of natriuretic contraction of plasma volume32 induced by supplemental K+ by its direct reduction of renal tubular reabsorption of Na+.34 However, it also seems likely that the decrease in GFR induced by KHCO3 reflects a decrease in an otherwise increased Poc and Re. Such decreases may be clinically relevant. In hypertensive patients, it has been observed that a prompt decrease in GFR and FF induced by the initiation of antihypertensive therapy is associated with a decreased rate of loss of renal function during continued treatment,35 possibly by decreasing intraglomerular pressure.

In NaCl-loaded SS blacks, it remains to be determined whether supplementing dietary K+ with KHCO3 has antipressor and GFR- and FF-reducing effects not shared by KCl. In SS human hypertension, the pressor effect of NaCl requires its Cl− component36; NaHCO3 has attenuated hypertension.37 In experimental animals, dietary Cl− can have its own pressor38,39 and renal vasoconstrictive effect,40 which may involve both efferent and afferent arterioles.41 In the SS, stroke-prone spontaneously hypertensive rat fed a normal NaCl diet, supplemental KHCO3 attenuated hypertension whereas supplemental KCl exacerbated it.39 Such selective Cl− sensitivity is likely to be mediated in part by renal vasoconstrictive dysfunction.39 In NaCl-loaded SS blacks, KCl may then have a lesser antipressor effect than KHCO3 and induce a lesser decrease in GFR and FF. Also, in SS blacks, Cl− may contribute to the pressor effect of dietary NaCl, not only by complementing Na+ in the expansion of plasma volume caused by salt36 but also by inducing renal vasoconstriction that both restricts the riddance of that expansion and directly participates in increasing peripheral vascular resistance.

In summary, in SS blacks, we find that dietary NaCl loading induced renal vasoconstriction whose extent varied directly with that of the attending pressor effect of NaCl. Supplemental KHCO3 abolished the pressor effect of NaCl without affecting the NaCl-induced reduction of RBF. However, supplemental KHCO3 reversed an NaCl-induced increase in FF and induced a substantial decrease in GFR that could reflect abolishment of an NaCl-induced increase in intraglomerular pressure.

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17. Schmidlin et al February 1999 639


NaCl-Induced Renal Vasoconstriction in Salt-Sensitive African Americans: Antipressor and Hemodynamic Effects of Potassium Bicarbonate
Olga Schmidlin, Alex Forman, Masae Tanaka, Anthony Sebastian and R. Curtis Morris, Jr

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