Role of Sodium in Hypertensive Cardiac Hypertrophy

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SUMMARY. Cardiac hypertrophy in systemic hypertension may not result simply from increased afterload. Previous studies indicate that factors other than blood pressure may influence cardiac hypertrophy. We evaluated the effects of dietary sodium restriction in two-kidney one-clip renal hypertensive rats. After the renal artery had been clipped, the rats received a normal diet until hypertension was established; thereafter, a sodium-deficient diet was instituted in one group. Clipped rats on a regular diet had significantly higher systolic blood pressures than sham-operated controls (205 ± 9 vs. 129 ± 1 mm Hg, respectively). Sodium restriction did not reverse hypertension (190 ± 8 mm Hg), but led to a significant reduction of relative heart weight compared to rats on the normal diet (2.94 ± 0.24 vs. 3.86 ± 0.23 mg/g, respectively; P < 0.01). The hypertrophied hearts of animals on the regular diet showed depressed tissue catecholamines (significant only for norepinephrine); sodium restriction resulted in a restoration to normal levels. Thus, we demonstrated a dissociation of blood pressure and cardiac hypertrophy in the two-kidney one-clip model, similar to previous findings in other models. Our results support the concept that factors other than blood pressure contribute to cardiac hypertrophy. Dietary sodium intake appears to be one such factor. In addition, a possible role of the sympathetic nervous system is suggested. (Circ Res 57: 610–617, 1985)

CARCI incapacitated by systemic hypertension does not appear to be simply a functional response of the myocardium to the mechanical stress of increased afterload. Workers in our laboratory, as well as other investigators, have demonstrated a dissociation of cardiac hypertrophy and blood pressure in various animal models (Sen et al., 1974; Tomanek et al., 1979; Fernandez et al., 1984). Similarly, a lack of correlation between severity of hypertension and cardiac hypertrophy has been reported in humans (Gross and Jezer, 1949; Grant, 1953; Ibrahim et al., 1981; Fouad et al., 1982). These findings have led to the speculation that factors other than blood pressure may regulate cardiac hypertrophy (Gross and Jezer, 1949; Grant, 1953; Sen et al., 1974; Ishise et al., 1980). The sympathetic nervous system may be one factor. (Tarazi et al., 1982).

In contrast, a similar dissociation of blood pressure and cardiac hypertrophy has not been shown to date in two-kidney one-clip (2K-1C) renovascular hypertension, a model thought to depend mainly on the renin-angiotensin axis (Davis, 1977) and on changes in water and sodium homeostasis (Swales et al., 1972; Moehring et al., 1975). Studies in this model so far have always shown a positive correlation of blood pressure and heart weight during both development and regression of cardiac hypertrophy (Sen et al., 1981).

We conducted the present study to reexamine the 2K-1C model of renovascular hypertension for evidence of factors other than blood pressure influencing cardiac hypertrophy. Since a possible role of sodium balance in the 2K-1C rat has been suggested, we examined the effects of dietary sodium restriction on cardiac hypertrophy in this model. We were able to document a dissociation of blood pressure and cardiac hypertrophy previously unreported in the 2K-1C rat: sodium restriction resulted in reversal of cardiac hypertrophy but did not lower blood pressure. Thus, dietary sodium intake may play a role in the pathogenesis of cardiac hypertrophy in this model. Furthermore, our findings also suggest a possible role of the sympathetic nervous system in this process.

Methods

Preparation of Animals

Male Wistar rats weighing 125–150 g were obtained commercially (Hilltop Farms). After reaching 150–175 g of body weight, the animals underwent left renal artery clipping with a 0.2-mm (internal diameter) silver wire clip under light ether anesthesia. We prepared an equal number of sham-operated controls, in which the renal artery was isolated but not constricted. The right kidney remained untouched in all animals. Subsequently, the rats were housed three per cage with free access to regular rat chow (Purina; [Na+] = 177 mEq/kg [Cl−] = 142 mEq/kg) and tap water.

Experimental Protocol (Fig. 1)

We had determined in pilot studies that blood pressure rises progressively during the first 4 weeks after renal artery clipping; thereafter, it stabilizes at hypertensive levels of about 190–210 mm Hg, as measured by tail-cuff
plethysmography. Therefore, animals were maintained on a regular diet until 4 weeks after surgery, at which time we divided the clipped, hypertensive (H) and sham-operated control (C) animals into eight separate groups (Fig. 1). Two groups, H1 and C1, continued to receive regular rat chow until they were killed, 12 weeks after operation. In two other groups, H2 and C2, we instituted a sodium-deficient diet (Teklad; [Na+] = 7 mEq/kg, [Cl−] = 149–154 mEq/kg) and maintained it for the next 8 weeks, again completing a 12-week protocol. Two additional groups, H1a and H2a, were subjected to a protocol identical to that of groups H1 and H2, but were killed earlier (between week 9 and 10). Finally, two groups, H3 and C3, were sacrificed at 4 weeks and served as controls for the degree of cardiac hypertrophy present before dietary manipulation.

Analytical Methods

Determination of Blood Pressure and Heart Rate

We measured systolic arterial blood pressures using the tail cuff method. This method has previously been validated in our laboratory (Sen et al., 1974). Using a Gould biotachometer, we simultaneously determined heart rate. The same investigator performed all measurements, at approximately the same time of the day, twice weekly and was unaware of the treatment group. Concomitantly, we also recorded body weights.

Tissue Catecholamine Preparation

After the animals were killed by decapitation, the hearts were rapidly excised, rinsed in saline, and blotted dry. The atria and great vessels were removed flush with the base of the heart. We determined the combined left and right ventricular weight (heart weight) to the nearest milligram and homogenized it with a polytron-tissue-homogizer. After the addition of 200 ng of dihydroxybenzylamine (DHBA), the internal standard, each sample was centrifuged at 20,000 g for 20 minutes at 4°C. To extract catecholamines from the supernatant, we used the alumina adsorption technique (Anton et al., 1962) at pH 8.7 and eluted with 0.2 N acetic acid. The samples were frozen in aliquots until analysis.

Catecholamine Determinations

After thawing and adding an antioxidant (Na2S2O5) and a chelating agent [(sodium-ethyldiamine tetraacetic acid (EDTA)], we loaded each sample onto a C18 reverse phase column (Novapak, 5-μm particle size, Millipore-Waters), using a Waters intelligent sample processor (WISP). Monochloroacetic acid (0.7 m) containing 1 mM sodium-EDTA, 2 mM sodium heptane sulfonate, and 3.3% (vol) methanol at pH 3.0 constituted the isocratic mobile phase, which was pumped at a rate of 1 ml/min by a Waters 600-A pump. We had previously adapted an amperometric electrochemical detector system (Bioanalytical Systems) for quantification of catecholamines. Using this system, we can detect catecholamine concentrations as low as 1 nm. A Waters data module served to record and integrate the signals from the amperometric detector. We prepared fresh external standards each day for norepinephrine (NE), epinephrine, dopamine, and DHBA. In preliminary studies, we had established a close correlation between recovery of internal standard and endogenous catecholamines. Catecholamine concentrations and contents were calculated according to recovery of the internal standard for each sample separately.

Plasma Renin Activity

We collected blood from the trunk for the first 4 seconds after decapitation in tubes wetted with NH4-EDTA. After centrifugation, plasma renin activity was determined by the method of Boucher et al. (1978), using an exogenous renin substrate prepared from plasma of bilaterally nephrectomized rats.

Measurement of Urinary Sodium Excretion

To demonstrate the effectiveness of dietary sodium restriction, we determined urinary sodium excretion. Animals were housed singly for several days in metabolic cages which allowed collection of urine which was not contaminated by food or feces. During these studies, the rats received their respective diets in pulverized form. We calculated total urinary sodium excretion from recorded daily urine volumes and urinary sodium concentrations which were assayed on a flame photometer (Instrument Laboratory 343).

Serum Electrolyte Analysis

Blood was collected at sacrifice, allowed to clot, and centrifuged. We determined serum sodium concentrations

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**Figure 1.** Experimental protocol. Each bar represents a group of clipped (H) or sham-operated (C) animals. Hatched portions of bars indicate administration of regular diet, open portions indicate administration of sodium-deficient diet. H1/C1: regular diet for 12 weeks. H1a: regular diet for 9.5 weeks. H2/C2: regular diet for 4 weeks, then sodium-deficient diet for 8 weeks. H2a: regular diet for 4 weeks, then sodium-deficient diet for 5.5 weeks. H3/C3: regular diet for 4 weeks.
on the same apparatus used for urinary sodium concentrations.

Tissue Water Content

A 100- to 200-mg tissue aliquot was removed from the apex of each heart and desiccated by repeated lyophilization until minimal weights remained constant on successive determinations. We determined tissue water content in percent by using the formula \[100 - \left(\frac{\text{dry weight}}{\text{wet weight}}\right) \times 100\].

Statistical Analysis

We calculated mean values and standard errors of the mean (SEM) for each group. Using the PROPHET computing system, analysis of variance was then performed (PROPHET Statistics Manual, 1980). Comparisons between individual groups are based on Student's t-test, Newman-Keuls multiple range test, or Kruskal-Wallis test, as was appropriate. Frequencies were compared by partitioned \(\chi^2\) test. We tested for correlations by linear regression analysis. For comparisons of cardiac mass we used absolute (i.e., combined right and left ventricular) weight as well as relative heart weight by calculating the ratio of heart weight to body weight. For statistical analyses, we expressed blood pressure as the mean of the average systolic blood pressure during the period of established hypertension from week 4 until week 12 for each animal. We chose this representation of blood pressure after pilot studies had shown that regression of cardiac hypertrophy occurs quite slowly under the experimental conditions used. This suggested that average blood pressure over time was a more relevant parameter than blood pressure at the end of the experiment. However, the point to be demonstrated by Groups H1a, H2a, H3, and C3 required use of blood pressure values at the time of sacrifice, and the mean of the last two readings was used. All data are expressed as means ± SEM. Statistical significance was defined as \(P < 0.05\). We have not repeated \(P\) values in the text when they appear in a table. Lack of a \(P\) value indicates that no significant differences exists.

Results

Body weight

All animals showed a normal pattern of growth. No differences between dietary groups occurred during experiments. Naturally, body weights at the time of sacrifice (Table 1) were lower in animals killed at a younger age (groups H3, C3, H1a, and H2a), but were not different among all groups sacrificed at 12 weeks.

Urinary and Serum Sodium Determinations

Animals receiving the low-sodium diet showed suppression of 24-hour urinary sodium excretion to extremely low levels, compared to rats on a regular diet (0.03 ± 0.02 vs. 1.84 ± 0.84 mEq/rat/24 hours, respectively; \(P < 0.001\)). However, we found no differences in serum sodium concentrations between animals on sodium-deficient and normal diets [137.7 ± 0.7 vs. 137.7 ± 1.6 mEq/liter, respectively; not significant (NS)].

Blood Pressure and Heart Rate

During the first 4 weeks after clipping, all animals showed a progressive rise in blood pressure (Fig. 2). Thereafter, blood pressure stabilized at about 190–210 mm Hg. No reduction in blood pressure occurred after the institution of the sodium-deficient diet.
diet in group H2. Blood pressure in these animals remained at unchanged, significantly elevated levels for the duration of the experiment. Means of average blood pressures during the period of established hypertension from week 5 until week 12 (Table 1) show no significant difference between groups of clipped animals on normal and sodium-deficient diet (205 ± 9 vs. 190 ± 8 mm Hg, respectively). The difference between clipped and sham-operated animals, all of which remained normotensive, was highly significant. We found no differences in blood pressures between the two sham-operated groups (129 ± 1 vs. 136 ± 2 for groups C1 and C2, respectively). A small but significant rise in blood pressure toward the end of the experiment in hypertensive animals on regular diet (group H1) became evident when the code was broken at the end of the experiment; no such increment occurred in sodium-restricted rats. The concern that this difference in blood pressure might represent a confounding factor for the interpretation of changes in heart weight prompted the addition of groups H1a and H2a to the study. These animals showed the same degree of hypertension as groups H1 and H2 and had blood pressures not different from each other (H1a: 206 ± 10 and H2a: 198 ± 6 mm Hg) at the time of sacrifice.

No differences in heart rate occurred among the experimental groups (Table 1).

Heart Weights

At sacrifice, we found a similar, significant degree of cardiac hypertrophy in groups H3 and H1, the two groups of clipped rats which had received the regular diet for 4 and 12 weeks ([4.26 ± 0.4 and 3.86 ± 0.23 mg/g, respectively (Table 1)]. These findings indicate that cardiac hypertrophy was already established 4 weeks after clipping, and maintained without major change thereafter. In contrast, despite their unaltered and marked hypertension, animals receiving the sodium-deficient diet (group H2) showed significantly lower relative heart weights. Their heart weight:body weight ratios were slightly, but not significantly, higher than those of normally fed controls (2.94 ± 0.24 vs. 2.38 ± 0.06 mg/g, respectively). Similarly, relative heart weights in group H2a were significantly lower than in the corresponding group H1a (3.52 ± 0.12 vs. 3.98 ± 0.13 mg/g, respectively), although the differences after 5 weeks of sodium restriction were not as pronounced as they were after 8 weeks.

Absolute heart weights, similar to heart weight:body weight ratios, were significantly lower in sodium-restricted animals (group H2) than in normally fed clipped rats (group H1) (1.37 ± 0.08 vs. 1.64 ± 0.08 g, respectively; Table 1). Absolute heart weights at 4 weeks after clipping (1.33 ± 0.05 g, group H3) and an additional 8 weeks of sodium restriction (group H2) were almost identical. Again, data for groups H1a and H2a mirror those for groups H1 and H2.

Regression analysis confirmed a significant positive correlation of blood pressure and relative heart weight for animals on regular rat chow (r = 0.881); this could not be shown for the sodium-restricted animals (r = 0.442). The difference between the two correlation coefficients is significant (P < 0.025).

Tissue Water Contents

By comparing wet and dry heart weights, we found no significant differences in tissue water contents between animals on normal and sodium-deficient diet (75.3 ± 0.2% vs. 75.3 ± 0.4%, respectively; NS).

Myocardial Catecholamines (Table 2)

Hypertensive animals receiving the regular diet showed significant reductions in cardiac norepinephrine concentrations and contents. Administration of the sodium-deficient diet resulted in a restoration to values of normotensive controls. Among sham-operated animals, we saw no changes after sodium restriction. Similar changes were observed for epinephrine. Dopamine concentrations showed the same pattern, whereas dopamine contents in-
increased to values significantly above baseline (group C1) in the hypertensive sodium-restricted group (group H2).

**Plasma Renin Activity (Table 2)**

Normal plasma renin activities were demonstrated only in the sham-operated animals on a regular diet (group C1, 29 ± 6 ng/ml per hr). Hypertensive and normotensive sodium-restricted rats showed similar elevations (group H2: 105 ± 31 ng/ml per hr; group C2: 105 ± 44 ng/ml per hr, respectively), as did the clipped animals on a normal diet (group H1, 70 ± 17 ng/ml per hr).

**Survival**

Preliminary studies had shown that, in 2K-1C rats receiving a regular diet, the rate of survival beyond 6–8 weeks after clipping is lower than in sodium-restricted animals. The six animals in group H1 represent the survivors of a group of 14 rats originally prepared. In contrast, none of the hypertensive rats receiving the sodium-deficient diet died prematurely. This difference in mortality (42% vs. 0%) reaches statistical significance ($P < 0.01$).

**Discussion**

Cardiac hypertrophy in systemic hypertension may be induced and maintained by factors other than blood pressure. The demonstration of a dissociation between blood pressure and cardiac hypertrophy in several animal models of systemic hypertension (Sen et al., 1974; Tomanek et al., 1979; Fernandez et al., 1984), as well as in essential hypertension in humans (Gross and Jezer, 1949), has led to speculations about the existence of factors which, present during states of heightened hemodynamic demands, may serve at the molecular level as a trophic stimulus for the myocyte (Sen et al., 1974; Tomanek et al., 1979). If one or more such factors indeed represents the common mediators of cardiac hypertrophy, then direct or indirect evidence for their existence ought to be found in all forms of cardiac hypertrophy. In the present study, we were able to demonstrate the reversal of cardiac hypertrophy despite persisting hypertension in the 2K-1C model of renal hypertension; this adds yet another model of systemic hypertension to the list of those in which a similar dissociation has been observed.

We observed no antihypertensive effects of sodium restriction in our experiments. This corresponds with several previous studies of this model in which established hypertension remained unaffected by the institution of a sodium-deficient diet (Redlaf and Tobian, 1953; Thurston and Swales, 1976; Munoz-Ramirez et al., 1980). Work by other investigators (Miksche et al., 1970; Moehring et al., 1975; Gavras et al., 1975) suggests, though, that sodium may play a certain role in this model. The failure of our sodium-restricted animals to show the same small rise in blood pressure as the untreated rats toward the end of the experiment may be related to these observations.

Our experiments indicate that dietary sodium restriction may reverse cardiac hypertrophy; this represents a new and previously unreported finding. Whereas numerous studies address the importance of sodium in hypertension, very few authors comment about its effects on the heart. Even fewer studies specifically deal with the role of sodium in cardiac hypertrophy; this sparsity of data makes interpretation of our results difficult and, by necessity, speculative. Regression of cardiac hypertrophy after sodium restriction has been demonstrated in both renoprival (Kazda et al., 1971) and deoxycorticosterone acetate (DOCA)-salt hypertension (de Champlain et al., 1968). However, in these studies, the concomitant fall in blood pressure precludes conclusions about independent effects of sodium on myocardial mass. Munoz-Ramirez et al. (1980), on the other hand, found no effects of sodium restriction on either blood pressure or heart weight in 2K-1C rats. However, major differences in the experimental design, namely, the duration of sodium restriction, make it difficult to compare this study with ours. Relative heart weights were significantly decreased from pretreatment levels after 8 weeks of

<table>
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<tr>
<th>Group</th>
<th>Noradrenaline</th>
<th>Epinephrine</th>
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<tr>
<td></td>
<td>(ng/g)</td>
<td>(ng/heart)</td>
<td>(ng/g)</td>
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<tr>
<td>H1</td>
<td>456 ± 51*</td>
<td>740 ± 38*</td>
<td>12 ± 2*</td>
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<tr>
<td>H2</td>
<td>858 ± 96</td>
<td>1206 ± 119</td>
<td>21 ± 3</td>
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<tr>
<td>C1</td>
<td>1009 ± 57</td>
<td>1139 ± 57</td>
<td>27 ± 4</td>
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<td>C2</td>
<td>1034 ± 46</td>
<td>1244 ± 44</td>
<td>22 ± 2</td>
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con, concentration; cont, content.

H1/C1: hypertensive/control animals on regular diet for 12 weeks. H2/C2: hypertensive/control animals on sodium-deficient diet week 4–12. Results are expressed as means ± SEM. No data were obtained in animals sacrificed 4 and 9 1/2 weeks after operation.

* $P$ less than 0.01 vs H2, C1, and C2.

† $P$ less than 0.01 vs H1, C1, and C2.
sodium restriction. However, when expressed as absolute heart weights, no significant change was demonstrated. An arrest of further growth with persistence of changes characteristic of hypertrophy or, more likely, regression of hypertrophic changes and concomitant normal growth could account for this finding. Future morphological and biochemical studies will help to clarify this.

We observed a small yet statistically significant difference in blood pressure between clipped animals on regular and on sodium-deficient diets during the last 3 weeks of the study. A mild increment in the blood pressure of normally fed rats toward the end of the experiment accounted for this finding. Since blood pressure in the sodium-restricted group remained at unattenuated hypertensive levels, one cannot relate the reversal of cardiac hypertrophy seen in these animals to this difference. The data from groups H1a and H2a, demonstrating regression of cardiac hypertrophy without any difference in blood pressure, confirm that the effects of sodium restriction on cardiac mass are indeed independent of blood pressure. In agreement with findings by others (Marcus et al., 1977), these results also support our impression that the reversal of cardiac hypertrophy is indeed a rather slow process. Hence, it appears that our decision to use time-averaged blood pressures, rather than values obtained at the termination of the experiment, as the relevant hemodynamic parameter, is justified.

Our data do not allow us to pinpoint the mechanism by which sodium restriction induced the reversal of cardiac hypertrophy. Conceptually, sodium homeostasis may affect the myocyte directly on an ionic basis or, more importantly, through modulation of any of a variety of neurohumoral effector systems. Vasopressin (Moehring et al., 1977), the prostaglandins (Tobian et al., 1974; Fujita et al., 1974), the proposed natriuretic factor (Mizukoshi et al., 1972; Haddy, 1979), and the renin-angiotensin system all have cardiovascular effects and are known to be influenced by the state of sodium balance. Clearly, much additional work is needed to explore these possibilities.

Significant alterations in indices of sympathetic nervous function occurred in our experimental animals. Changes in total organ catecholamine contents cannot be explained by dilutional effects, and appear to indicate true changes in catecholamine homeostasis. The possible importance of these changes is stressed by previous evidence for the role of the sympathetic nervous system in cardiac hypertrophy. Such a role was initially suggested by the isoproterenol model of cardiac hypertrophy (Aldermann and Harrison, 1970); subsequent findings of altered sympathetic activity in the hypertrophied hearts of spontaneously hypertensive rats (SHR) (Ishise et al., 1980) and of animals with deoxycorticosterone acetate (DOCA)-salt hypertension (de Champlain et al., 1968), aortic constriction (Fischer et al., 1965), and pulmonary artery banding (Schmid et al., 1982) have supported the view that sympathetic tone exerts a trophic stimulus on the heart (Tarazi et al., 1982). In the 2K-1C model, current evidence does not support an important role of the adrenergic system. Previous work has emphasized the lack of response to different sympatholytic agents in this model (Dargie et al., 1977). However, a few observations seem to indicate a possible contribution of the sympathetic system in the 2K-1C model, too. Two groups (Drews et al., 1968; Kuwajima et al. 1982) have documented antihypertensive effects in 2K-1C rats after they had been treated with three-α-methylnorepinephrine and methyldopa, respectively. Thus, increased sympathetic nervous tone may, after all, be a factor in this model, possibly exerting a growth-promoting effect and concomitantly leading to depletion of tissue stores of sympathetic neurotransmitters. Restoration of normal catecholamine homeostasis might then be associated with reversal of cardiac hypertrophy. These hypotheses are indeed compatible with our findings, and certain aspects of the complex interrelationship of sodium and sympathetic nervous function (Vollmer, 1984) even allow one to infer a role of dietary sodium restriction in this process. However, the cardinal question whether sodium restriction reversed cardiac hypertrophy and raised cardiac catecholamines independently, or whether it led to changes in sympathetic tone, which, in turn, contributed to the reversal of cardiac hypertrophy, remains open; further work is needed to answer this question.

We found significant elevations in cardiac dopamine contents associated with reversal of cardiac hypertrophy in sodium-restricted animals. Very little is known about myocardial dopamine in the 2K-1C model (Naik et al., 1982); therefore, interpretation of our findings is difficult. They may again simply reflect a change incidental to sodium restriction; the trend toward higher dopamine values in sham-operated animals seems to support this. Alternatively, the increased dopamine values may actually reflect a rise in plasma dopamine concentrations, since we did not perfuse the hearts to clear them from blood. The unique cardiovascular properties of dopamine invite speculations about a possible meaning of our findings in this context: relaxation of the splanchnic and renal vasculature causing a fall in total peripheral resistance (which may occur despite the unaltered systolic pressures we found) may have attenuated the signal leading to activation of hypertrophy-maintaining mechanisms.

We observed a significant reduction in mortality in hypertensive animals on a sodium-restricted diet. Reversal of cardiac hypertrophy with improvement of hemodynamic function may have played a role; however, in future studies, possible differences in the incidence or severity of renal and cerebrovascular disease will have to be excluded to confirm this.
The present study has certain shortcomings, many of which have already been mentioned. It may be important, in future studies, to correlate cardiac hypertrophy with more sensitive parameters for afterload than systolic blood pressure. Comparison of right and left ventricular characteristics may more clearly delineate the effects of systemic hypertension and treatment. Determination of humoral factors influenced by sodium may shed light on the possible indirect effects of sodium restriction. Importantly, catecholamine turnover studies are needed to interpret the functional meaning of the observed changes. Finally, repetition of our experiments in other models of cardiac hypertrophy will allow us to distinguish whether the effects of sodium restriction are particular to the 2K-1C model or are more general in nature.

The findings of this study lend added support to the concept that factors other than blood pressure influence the development, maintenance, and regression of cardiac hypertrophy. In our experiments, dietary sodium restriction was associated with a reduction of relative heart weights in clipped animals to values not different from normotensive, sham-operated controls. This reversal of cardiac hypertrophy occurred despite unchanged, persistent hypertension. Also, our results appear to support a role of the sympathetic nervous system in cardiac hypertrophy, similar to other models of systemic hypertension. Thus, our findings suggest that, in addition to its effects on blood pressure in many forms of hypertension, sodium may also play an independent role in the pathogenesis of cardiac hypertrophy. Further definition of this role will enhance our understanding of cardiac hypertrophy and, ultimately, may have implications for prevention and treatment of this condition.

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