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Effect of Weight-Reducing Diet on the Blood Pressure of Spontaneously Hypertensive Rats (41223)

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Abstract. Spontaneously hypertensive rats were placed on weight-reducing diets either by limiting regular feedings to twice weekly or by providing half the normal ration daily. Significant reductions in body weight and blood pressure were observed at 2, 4, and 6 weeks after beginning the diet. Blood pressure fell despite maintenance of a normal or elevated sodium intake indicating that the reduction was not secondary to decreased sodium intake. Reinstitution of a normal food intake resulted in a return of body weight and blood pressure within 3 weeks.

A fall in blood pressure usually accompanies a reduction in body weight. This observation has been documented in obese patients on weight-reducing diets (1, 2) and from populations enduring severe caloric restriction such as during the siege of Leningrad in World War II (3). Although a relationship between reduced food intake and lowering of blood pressure is generally accepted, a controversy exists as to whether it is secondary to a reduction in calories or in sodium (4, 5). The present study was designed to examine the effect of weight reduction on the blood pressure of the Kyoto strain of spontaneously hypertensive rat (SHR). To our knowledge there have been no previous studies of the effects of weight reduction on the hypertension of the SHR. In the present investigation, salt intake was maintained at or above control levels during the period of caloric restriction.

Methods. Both male and female 4- to 5-month-old SHR were included. The diet of the rats consisted of a commercial feed (Wayne Lab-Blox) which contained 14.5% protein and 4.1% fat. The normal average daily consumption of this diet was approximately 21 g in males and 14 g in females. At the beginning of the experimental period, body weight averaged 325 g in the males and 195 g in the females.

The animals were randomly assigned to one of four regimens as follows: Group I, a control group which received daily food without reduction in quantity and tap water for drinking. Group II, an experimental group which received the usual ration of Lab-Blox as was given to Group I but it was fed only twice weekly. Group II animals also received 0.4% NaCl in the drinking water when food was withheld. Group III received the same ration of food as Group II but they continued to drink tap water. Group IV received half the normal food ration daily and 0.2% NaCl solution in place of drinking water. The NaCl solutions used in Groups II and IV were more than sufficient to maintain sodium intake at or above control levels.

The reason for adding NaCl to the drinking water was to replace the reduction in sodium intake that resulted from the restricted diets. Animals on unrestricted intake of Lab-Blox have an average sodium intake of 82 mg per day in males and 55 mg in females. The average water intake was about 50 ml per day in males and 40 ml in females. Therefore, the approximate daily sodium intake in Group II animals who were given 0.4% salt solution to drink was 82 mg in males and 66 mg in females. The Group IV animals received approximately half this amount in their drinking water which was calculated to replace the sodium reduction in their diet.

The first three groups each consisted of eight males and five females while Group IV comprised four male rats. Blood pressure was determined by the tail plethysmographic technique; weights were taken when the diet was begun and at 2 and 4 weeks after its initiation. Following the fourth week Groups II and III were re-

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turned to normal daily feedings plus tap water. When the rats attained weights similar to those of the control animals their blood pressures were again determined. Group IV was allowed to continue on their diet regimen for a period of 6 weeks in order to observe the effect of a more prolonged but less restrictive diet on blood pressure.

Results. There was a considerable loss of weight in both male and female rats in Groups II and III after 2 weeks of reduced food intake (Table I). The males continued to lose weight throughout the period of food restriction reaching an average level which was 31% below control weight by the fourth week. Female rats on the other hand stabilized their weight after the second week of food reduction.

The blood pressure of the male rats in Groups II and III fell significantly, averaging 16% below that of the control rats after 4 weeks of food restriction (Table I). The range of blood pressure in the male control rats was 166–227 mm Hg prior to the experiment and rose to 178–245 after 4 weeks. The method of statistical analysis used was the unpaired two-tailed t test. The P values given in the table are based on the absolute values. The blood pressure of the female rats in Groups II and III averaged only slightly lower than that of the control rats and the difference was considerably less than in the males and was significant only at 2 weeks after beginning the diet.

The correlation coefficient between change in body weight and change in blood pressure was determined using all of the experimental groups plus the controls. At 2 weeks there was a significant correlation ($P < 0.001$) between these two variables with $r = 0.69$. After 4 weeks the correlation was still significant ($P < 0.001$) and $r = 0.62$. However, the correlation coefficient was not significant between change in body weight and change in blood pressure when the analysis was done within each experimental group.

The reduced feedings were terminated after 4 weeks at which time Group II and III animals were given food and tap water *ad libitum*. With refeeding, the body weights and blood pressures increased rapidly and

TABLE I. EFFECT OF WEIGHT REDUCTION ON BLOOD PRESSURE OF SPONTANEOUSLY HYPERTENSIVE RATS

Group	Percentage change body weight					Percentage change blood pressure				
	Control	2 weeks	4 weeks	6 weeks	Refeeding, 3 weeks	Control	2 weeks	4 weeks	6 weeks	Refeeding, 3 weeks
(Males)										
I	318 ± 22.9[a]	+2.5	+5.0	+7.5	+8.5	198 ± 18.3[b]	+5.5	+6.6	+7.8	+9.1
II	321 ± 17.9	−20.0****	−32.0****		+2.5	199 ± 13.2	−9.0***	−9.0***		+8.5
III	322 ± 20.3	−19.0****	−30.0****		+6.2	208 ± 7.9	−10.0***	−9.6*		+2.9
IV	340 ± 24.4	−3.2	−13.2**	−20.3****		198 ± 21.9	−1.0	−8.5**	−12.1***	
(Females)										
I	189 ± 4.6	+3.7	+8.5		+10.6	177 ± 7.5	+7.9	+2.8		+6.2
II	198 ± 7.4	−26.8****	−25.3****		+6.1	175 ± 8.5	−2.9***	−1.7		−1.1
III	198 ± 11.6	−24.7****	−22.2****		+3.0	178 ± 4.0	−7.9***	+1.1		+0.6

[a] Mean grams ± SD.
[b] Mean mm Hg ± SD.
* $P < 0.05$.
** $P < 0.02$.
*** $P < 0.01$.
**** $P < 0.001$.

after 3 weeks reached levels insignificantly different from those of the control animals (Table I).

The male rats in Group IV who were placed on a diet less restricted in calories than Groups II and III exhibited a more gradual fall of body weight than the latter. The reduction averaged 13.2% after 4 weeks. Blood pressure fell 8.5%, which nearly approached the level of the Group II and III rats after 4 weeks. A further reduction in both body weight and blood pressure was observed after 6 weeks when there was an average fall of 12.1% in the rats receiving the diet (Table I). During the same 6-week period blood pressure in the control animals rose by an average of 7.8%.

Discussion. The present study indicates that the elevated blood pressure of the male SHR is reduced when the animal loses weight. A relationship between body weight and blood pressure was further shown by the prompt return of elevated blood pressure when the fasted animals were permitted an unrestricted diet; the rise in blood pressure paralleled the increase in body weight. The elevated blood pressure of the male SHR showed a significant reduction during the first 2 weeks after the animal loses weight. Beyond 2 weeks, however, and despite further loss of weight there was no further significant reduction of blood pressure. The reason for the lack of continued blood pressure reduction after the initial 2 weeks was not evident. However, it was not due to a change in the composition or type of food since only the quantity was altered as compared to the control. A more likely possibility is that the relationship between body weight and blood pressure is not linear over the entire range of body weight changes but rather they are related only with regard to moderate reduction. This suggests that there may be a minimal level of body weight below which further reductions in weight no longer are associated with additional falls in blood pressure.

There have been very few prior studies of the effects of weight reduction on hypertension in experimental animals. The only report we found was a study published in 1939 by Wood and Cash (2). These investigators reported a significant increase in body weight and blood pressure in both normal and renal hypertensive dogs fed a high fat diet.

The relationship between body weight and blood pressure in man, however, has been recognized for many years. As early as 1925, for example, it was found in life insurance applicants that elevated blood pressure was five times more frequent in overweight persons than in the applicants whose weight was normal (6). Brozek *et al.* investigated the effects of a semistarvation diet in normal volunteers. A 24% reduction in body weight was associated with a decline of 10.6% in systolic blood pressure (3). The relative magnitudes of these changes are similar to those we found in the SHR. More recently, Reisen *et al.* (7) found in overweight patients with mild uncomplicated essential hypertension that a diet which induced an average weight loss of 10.5 kg was associated with a return to normotension in 75% of the patients.

There was a considerable difference in this study on the effects of the diet in the two sexes. Females showed weight loss comparable to that of the males but much less reduction of blood pressure. Also, in contrast with the males the females showed little or no rise of blood pressure on refeeding. The reason for the resistance of the female rat's blood pressure to change in the presence of dietary restriction is not apparent. In the human the female seems equally responsive to weight reduction as the male (7). In a controlled trial Fletcher found a highly significant reduction in blood pressure in obese women following weight reduction (8). The significance of the difference remained after correcting for changes in arm girth.

The mechanism for the fall in blood pressure which accompanies weight reduction is not clear. On the basis of dietary experiments in a small number of hospitalized hypertensive patients Dahl concluded that the antihypertensive effect of food restriction was due to reduced salt intake rather than to lowered calories (4). Reisen *et al.* (7), on the other hand, maintained a high salt intake with his weight-reducing diet and still obtained significant reductions of blood pressure. The present studies in the SHR also indicate that the antihypertensive effect of weight-reducing diets cannot be ascribed to a lowered salt intake since the antihypertensive effect was not prevented by administering excess salt in the drinking water. While it is possible that the lowered salt intake associated with food restriction may have contributed in part to the antihypertensive effect of the diet it did not appear to be the major contributor. Watkin and his associates (9) found in humans that the degree of sodium restriction in the diet must be reduced to 400 mg/day or to one-tenth of the usual daily intake in order to obtain a significant antihypertensive effect. This degree of sodium restriction did not occur in the present study and may explain why the blood pressure falls were similar on the salt-supplemented and non-salt-supplemented rats on caloric-restricted diets.

Other possible mechanisms have been proposed. The release of catecholamines is suppressed during fasting in rats (10) suggesting that the fall in blood pressure may be due to reduced catecholamines. However, no work has been done to determine the importance of this change in catecholamines on the reduction of blood pressure that accompanies reduced food intake. Additional hypotheses that have been advanced to explain the association between obesity and hypertension include increase in blood volume and cardiac output (11) and abnormalities of adrenal steroid secretion (12). The SHR should provide a useful model for studying these and other possible mechanisms that might relate alterations in body weight with changes in blood pressure.

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