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Blood Pressure of Rats as Affected by Diet and Concentration of NaCl in Drinking Water[1] (39219)

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There is some question about the relation between dietary salt intake and the development of hypertension in human beings (1, 2). The demographic studies which have yielded strong correlations between salt intake and the incidence of hypertension (1, 2) have been proposed as evidence for a causal relationship between the two. This argument has been supported by the aggravation of hypertension when individuals are fed a high salt diet (3), and the reductions in blood pressure when a low salt diet is followed (4). Some investigators have provided evidence that other factors are more important than the salt intake in initiating human hypertension (5).

The early work on hypertension emphasized the possible role of salt in its etiology, some of the more recent suggestions appear to implicate the carbohydrate component of the diet. It is possible that Snapper's report (6) about the low incidence of hypertension among rice-eating peoples may have motivated Kempner to use the rice-fruit diet in treating his hypertensive patients. He observed a reduction in blood pressure when the hypertensive patients were changed from a regular hospital diet to a rice-fruit diet (7, 8). Later, Hatch *et al.* (9) established that the therapeutic effect of the diet was due to its low sodium content. Since that time, several investigators have been successful in producing hypertension in rats through administration of excess sodium chloride either in the diet or the drinking solution (9-15).

The carbohydrate component of the diet has received only cursory experimental attention in relation to hypertension. A difference between glucose and sucrose was reported when they were tested in aqueous solutions. Sucrose consumed by rats as aqueous saline solutions produced a more severe elevation in blood pressure than glucose-saline solutions (11). However, a diet composed largely of sucrose has not been examined for its effect on blood pressure.

It has been suggested that a high sucrose content in the diet of humans may hasten the onset of hypertension and cardiovascular disease, but substantial evidence in support of this theory has not been produced (16). The objective of the present study was to examine the possible relationship among the primary dietary components and the development of hypertension either with or without excess sodium chloride ingestion.

Materials and methods. Animals, diets, and drinking solutions. For Experiment 1, 64 male Osborne-Mendel (OM) rats were weaned at 21-24 days of age and divided into four groups of 16 rats each. All animals were housed individually in wire screenbottomed cages 18 × 18 × 25 cm. Room temperature was maintained at 23 ± 1°, and 12 hr of light followed by 12 hr of darkness were allowed in each 24-hr period. Activity was neither promoted or restrained.

Each group of rats was fed one of the following four diets: grain, a semipurified diet high in sucrose, a semipurified diet high in cornstarch, or a semipurified diet high in fat. The grain ration was selected as a control model for the study since the majority of investigations of blood pressure have been conducted with standard chow-type rations similar to the grain diet. The high carbohydrate diets were fabricated to be similar to the grain ration in protein, carbohydrate, fat, and fiber and to provide the same amount of kcal/g of protein consumed. The high fat diet was similarly fabricated to maintain the same kcal/protein ratio as the semipurified high carbohydrate diets. Composition of the grain ration and a represent-

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ative high fat ration has previously been described (17).

Each dietary group of rats was further divided into two groups of eight rats each. One group was given distilled, deionized water and the other a 2% NaCl solution. The feeding period lasted 10 weeks during which time weekly systolic blood pressure and pulse rates were recorded.

Because of a high rate of mortality among rats fed the semipurified diets and offered the 2% NaCl solution, Experiment 2 was conducted. Twenty-four rats were weaned at 21–24 days of age and divided into four groups of six rats each. Each group was fed one of the four diets used in Experiment 1. Rats were offered distilled, deionized water for the first 3 days postweaning, followed by a 1% NaCl drinking solution for 9 weeks. A 1.5% NaCl drinking solution was substituted during the tenth week and continued until Week 18 when the experiment was terminated.

Sodium intake. Rats were allowed to eat and drink *ad libitum*. Food intake records were kept weekly for each rat by weighing the full food cup at the beginning of each week and substracting from it, the weight of the cup at the end of the week. Correction for spillage was made by retrieving as much of the spilled ration as possible and adding this amount to the cup at the end of the week. Diets were analyzed for sodium so that the amount of dietary sodium ingested could be determined.

One-hundred-milliliter graduated cylindrical water bottles were used to quantitate the fluid consumed. The total amount of sodium ingested by each rat was the sum of that in the diet and the drinking solution.

Blood pressure. Blood pressure was determined weekly between 8 AM and 1 PM on the same day. This parameter was indirectly measured using a rubber lined, metal tail cuff and a pneumatic pulse transducer attached to a Desk Model Physiograph.[3] For the blood pressure estimation, the rats were put into a Plexiglas restrainer which was placed on a heating pad, the surface of which was maintained at a temperature of 33 ± 1°. The rats were acclimated to the heated restrainer for a period of 10 min to calm the animal and stimulate blood flow through the tail.

Statistical calculations. At the end of the experimental period a Student's *t* test (18) was used to determine significant difference between mean blood pressures of rats fed the grain ration and those fed the semipurified diets. Differences in cumulative sodium intakes were similarly analyzed.

Results. Blood pressure: Experiment 1. Rats fed the semipurified diets high in fat, cornstarch, or sucrose while drinking distilled, deionized water had mean systolic blood pressures of 114 ± 13, 117 ± 7, and 127 ± 9 mmHg, respectively, at the end of 10 weeks. Blood pressures of rats fed the grain ration were 109 ± 14 mmHg (Fig. 1A). All blood pressures were within the normal range, i.e., a systolic pressure less than 140 mmHg (19–21). However, blood pressure of rats fed the semipurified ration high in sucrose was significantly higher than blood pressures of rats fed grain ($P < 0.01$).

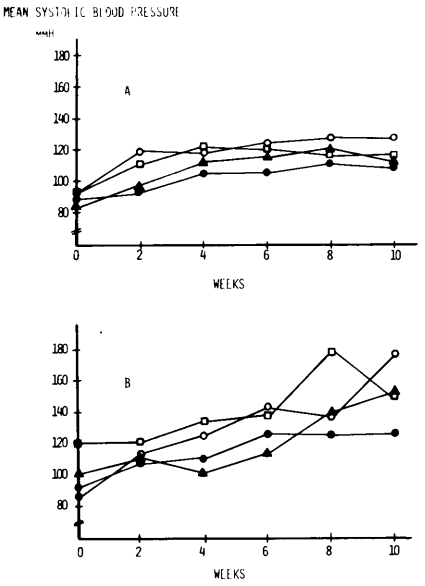

FIG. 1. Mean systolic blood pressures of male OM rats fed a grain ration, ●; or a semipurified diet high in sucrose, ○; cornstarch, □; or fat, ▲, for 10 weeks. (A) Rats consumed distilled, deionized water (n = 8 for each diet group). (B) Rats consumed a 2% NaCl drinking solution (n = 7 for grain; n = 2 for high sucrose; n = 4 for high cornstarch; and n = 2 for high fat fed group).

[3] Narco Biosystems, Houston, Texas.

Substituting a 2% NaCl drinking solution for deionized water increased the blood pressure of rats regardless of diet. By the tenth week of the experiment, rats fed the semipurified rations high in fat, cornstarch, or sucrose and drinking the saline solution had systolic pressures of 154 ± 8, 150 ± 20, and 178 ± 14 mmHg, respectively. Rats receiving the grain ration and 2% saline had a mean systolic pressure of 127 ± 20 mmHg. Compared to rats drinking deionized water, this was a mean increase in blood pressure of 18, 33, 33, and 51 mmHg for rats consuming grain and semipurified rations high in fat, cornstarch, and sucrose, respectively. The differences were significant ($P < 0.001$). A systolic blood pressure greater than 140 mmHg is considered by many investigators as indicative of hypertension (19-21). According to this criterion, all rats fed the semipurified rations could be classified as hypertensive. When tested at 10 weeks, rats fed the semipurified ration high in sucrose were the only ones with systolic pressures that were significantly greater than those of rats fed the grain ration ($P < 0.02$). However, it should be noted that at 9 weeks, rats fed the ration high in cornstarch had a mean blood pressure of 180 mmHg. Since there was high mortality among rats fed the semipurified diets, data represented only two or four rats per group. Therefore, a second experiment was conducted in which the concentration of NaCl in the drinking solution was reduced in an effort to decrease mortality.

Experiment 2. For rats offered a 1-1.5% NaCl solution for 18 weeks there were no statistical differences in final mean systolic blood pressures among diet groups (Fig. 2). Rats fed the grain or the semipurified diets high in fat, cornstarch, or sucrose had final mean pressures of 130 ± 15, 133 ± 13, 133 ± 9 and 140 ± 16 mmHg, respectively. Only those rats fed the high sucrose diet could be classified as mildly hypertensive. However, all blood pressures tended to increase with age, regardless of diet.

Sodium intake: Experiment 1. The kcal/sodium ratio was similar in each diet. Since there was not a significant difference in mean cumulative energy intake among groups of animals offered distilled, deionized water, it followed that total sodium intake also was not significantly different (Table I). Rats offered the 2% NaCl solution ate 42-80% of the food consumed by those offered deionized water, thereby also decreasing dietary sodium intake (Table I). However, fluid consumption increased threefold regardless of diet. This resulted in seven- to eightfold increases in cumulative mean sodium intakes, which ranged from 52.4 ± 7.5 to 57.0 ± 3.7 g. These values were not significantly different.

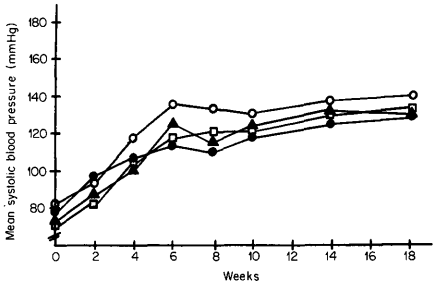

FIG. 2. Mean systolic blood pressures of male OM rats fed a grain ration, ● ($n = 7$); or a semipurified diet high in sucrose, ○ ($n = 5$); cornstarch, □ ($n = 7$); or fat, ▲ ($n = 6$), and offered a 1-1.5% NaCl drinking solution for 18 weeks.

Experiment 2. Food and fluid intakes were similar among rats in the different diet groups, and for this reason there was not a significant difference in total sodium intake whether expressed as an absolute value or relative to body weight (Table 1).

Discussion. Blood pressure of normal rats progressively increases with age before plateauing at a level of 100-120 mmHg for animals with a body weight of 200 g or more (22). In this study the blood pressure of rats fed the grain ration and distilled, deionized water followed this normal trend. In contrast, rats fed the semipurified rations experienced a more rapid rise in blood pressure before plateauing at a higher level than rats fed the grain ration. Such results imply that the type of diet influences blood pressure.

Blood pressure in rats, offered either of the salt solutions, were elevated compared to rats drinking distilled water, regardless of the diet. However, the trend toward increased blood pressure was the greatest among rats eating the semipurified rations rather than the grain ration. The ability of

TABLE I. CUMULATIVE SODIUM INTAKES OF MALE OM RATS FED A GRAIN RATION OR SEMIPURIFIED DIETS HIGH IN FAT, SUCROSE, OR CORNSTARCH WHILE CONSUMING ONE OF SEVERAL DRINKING SOLUTIONS.

Treatment	Cumulative sodium intake[a]	
	g/rat	g/100 g body wt.
Experiment 1[b]		
Distilled deionized water		
Grain (8)[c]	7.5 ± 0.7	2.0 ± 0.2
High fat (8)	7.0 ± 0.7	1.7 ± 0.2
High sucrose (8)	8.2 ± 0.6	1.9 ± 0.2
High cornstarch (8)	8.0 ± 0.8	2.1 ± 0.3
2% NaCl		
Grain (7)	53.9 ± 11.0	32.9 ± 23.4
High fat (2)	53.4 ± 1.3	26.5 ± 0.9
High sucrose (2)	52.4 ± 7.5	38.0 ± 21.7
High cornstarch (4)	57.0 ± 3.7	29.9 ± 9.9
Experiment 2[d]		
1-1.5% NaCl		
Grain (6)	56.7 ± 5.8	12.9 ± 1.3
High fat (5)	56.4 ± 9.9	11.7 ± 2.1
High sucrose (5)	66.7 ± 15.9	15.2 ± 3.6
High cornstarch (6)	61.5 ± 15.1	14.3 ± 3.4

[a] Mean ± standard deviation.
[b] Total for 10 weeks.
[c] Numbers in parentheses show number of animals in group.
[d] Total for 18 weeks.

excessive salt consumption to provoke hypertension in rats is well documented (2, 10–12, 15). The interaction between salt and other dietary components has not been as well established. Hall *et al.* (23) observed higher blood pressures in rats ingesting a sucrose-saline solution than in rats consuming a glucose-saline solution. Data from the present study are in agreement with Hall's, especially when comparisons are made between the rats fed the semipurified diet high in cornstarch, and those fed the diet high in sucrose and offered 1.0–1.5% NaCl solutions (Fig. 2). Rats fed the high sucrose diet responded with a higher blood pressure at a younger age than rats fed any one of the remaining semipurified diets or the grain ration. This was true despite failure to show a difference in sodium intakes among dietary groups.

Dalderup (24) noted a decreased life span and early onset of glomerulonephritis in Wistar albino rats when dietary sucrose was increased from 15 to 30% of the diet. In the present study, rats fed any of the semipurified diets while consuming the 2% NaCl solution had higher mortality rates than rats fed the grain ration. The incidence of kidney lesions is increased by feeding a sucrose diet (24) and in salt-induced hypertension (25). Winnie *et al.* (26) observed a higher percentage of fat in kidneys of rats fed a semipurified diet high in sucrose when compared to rats fed either a semipurified diet high in fat or grain. In addition, overfeeding in general has been shown to produce renal lesions and hypertrophy in rats (27).

Summary. In the first experiment, weanling rats were fed a grain ration or one of three semipurified diets high in fat, sucrose, or cornstarch. Rats in each dietary group were divided into two subgroups, one of which drank distilled deionized water whereas the other group drank 2% NaCl solution. Blood pressure and sodium intake were individually measured for each rat at weekly intervals for a 10-week period. Rats receiving the salt solution had higher mean blood pressures (127–178 mmHg) than rats offered distilled water (108–127 mmHg). When drinking solutions were the same, more severe rises in blood pressure occurred in rats fed the semipurified diets than in those rats fed grain. In a second experiment, rats were fed one of the four diets used in the first experiment; however, they received a 1% NaCl drinking solution for 9 weeks followed by a 1.5% NaCl solution for an additional 9 weeks. At Week 18, pressures among these groups of rats ranged from 136–140 mmHg, regardless of diet.

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