may affect absorption. While the drug was given i.m., significant bacterial alterations may have occurred in the relatively short period of these experiments. It has been observed that germ-free animals have impaired absorption and utilization of iron(6) and increased xylose absorption(7).

Tetracycline is capable of chelating with various multivalent ions including ferrous and ferric(8), and such chelates may either be poorly absorbed or may be more rapidly excreted following absorption than the free forms. The findings with parenterally administered ^{59}Fe (Table III) rule out increased excretory loss as the result of TC administration, but the effect on iron absorption is not known.

In considering interference with specific transfer mechanisms across the gut wall, it has been suggested that certain inhibitors of protein synthesis inhibit fat absorption by interfering with β-lipoprotein synthesis in the mucosal cells(2). TC may exert its effect by a similar mechanism since the dosages given are capable of inhibiting amino acid incorporation into proteins of the G.I. tract(1). However, we did not observe the accumulation of fat in epithelial cells described to have occurred with the other inhibitors of protein formation(2). Since i.m. TC causes local irritation with fluid accumulation, the possibility must be considered that hypovolemia occurred which could have depressed intestinal lymph and blood flow with consequent malabsorption. However, this hypothesis seems improbable since decreased intestinal perfusion should have impaired absorption of all nutrients; furthermore, severe mechanical trauma in the limbs of rats did not impair fat absorption (unpublished data).

Summary. Tetracycline administration to adult rats (250 mg per kg i.m.) was associated with impaired intestinal absorption of fat (as ^{131}I triolein) fatty acids (as ^{131}I oleic) and radioactive iron. The jejunal mucosa of the treated animals was microscopically normal and without lipid accumulation. D-xylose absorption appeared to be increased as the result of tetracycline treatment since urinary excretion was significantly greater than that of control. Vitamin B_{12} absorption was not affected. Possible mechanisms accounting for this differential effect are discussed.

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Comparative Effectiveness of Glucose and Sucrose in Enhancement of Hypersalimentation and Salt Hypertension.* (31491)

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Rats prefer drinking certain sugar solutions to water(1) and become hypertensive when given saline to drink(2-4). Consequently, the addition of several sugars in 5% concentration to a 1% saline solution increases the quantity of fluid and electrolyte consumed, and increases severity of salt hypertension in these animals(5,6). Although sucrose, fructose and one of two samples of maltose each were found to share this property, sucrose has thus far been the most efficacious(7,8). Curiously, the incorporation of honey is without effect upon either saline consumption or induction of hypertension(8). Since the ability of sugars to increase saline consumption is not a function of their inherent "sweetness"(8),

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is not clearly related to the caloric value said to dominate the ingestive habits of rats(9), and is at variance with the order of preference observed when they are added to water and tap water offered as a choice(1), studies on the effect of other sugars and sweetening agents on saline consumption are in progress. The present study is concerned with a comparison between sucrose and glucose, the latter reputed to be 75% as sweet as the former(10).

Materials and methods. Female rats of the Houston-Cheek strain were anesthetized, the right kidney removed, and divided into 4 groups. Group 1 consisted of 8 animals given distilled water to drink, Group 2 of 10 given 1% NaCl solution, Group 3 of 10 drinking a 5% sucrose 1% saline solution, and Group 4 of 10 drinking a 5% glucose 1% saline solution. All solutions were made with distilled water. The animals were individually housed in temperature-controlled quarters and received Purina laboratory chow *ad lib.* All animals were injected upon arrival in the laboratory, and weekly thereafter, with 0.2 ml of a 20,000 unit/ml penicillin and 25 mg/ml streptomycin solution to inhibit developement of respiratory infections.

Systolic blood pressure of unanesthetized animals was measured periodically by tail plethysmography and values above 150 mm Hg were taken to indicate hypertension. Fluid intake of each rat was measured on 3 consecutive days each week, and the average value taken to be indicative of the daily consumption for that week.

The animals were killed on the 34th experimental day, and various tissues and organs taken for weight and/or histology were placed in 10% neutral formalin. Organs, when fixed, were removed, blotted, trimmed, and weighed on an analytical balance.

Results. Growth. There was no difference in growth rate between the groups during the experiment and the terminal group average body weights were within an 8 g range.

Fluid consumption. The group average water intake of rats ranged from 26 ml/100 g/day in the first week to 20 ml/100 g/day at the end of the 5th week, no period differing from the one preceding or following by more than 5 ml/100 g/day. The comparable figures for those drinking saline were 45 ml/100 g/day and 37 ml/100 g/day, with the same weekly range.

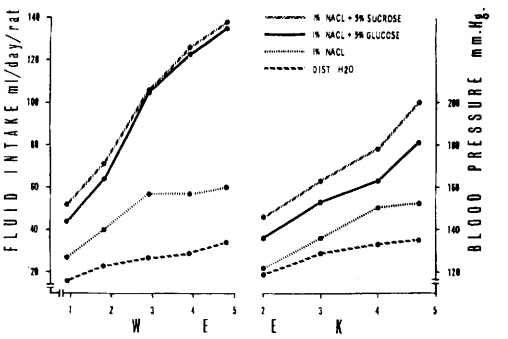

FIG. 1. Sequential development of changes in fluid intake and blood pressure of rats given various types of fluid to drink.

Rats drinking sucrose-saline consumed 72 ml/100 g/day at the outset and 86 ml/100 g/day terminally, with a weekly range of 10 ml/100 g/day; and those drinking glucose-saline 61 ml/100 g/day and 79 ml/100 g/day, with a range of 15 ml/100 g/day. Since neither the initial, final nor any of the weekly group average body weights differed significantly from those of any other, the statistical computations and graphical data to follow are given on an absolute rather than relative basis.

Saline consumption exceeded water consumption in each of the weekly periods ($P<.001$ or more), but even more glucose-saline or sucrose-saline solution was consumed than either water or saline in each period ($p<.001$ or more). More sucrose-saline than glucose-saline was consumed in the first week ($P<.05$). Thereafter there was no significant difference between the two in any period (Fig. 1). Although the consumption of water or saline increased at a rate slower than growth, the intake of glucose or sucrose and saline increased faster.

Blood Pressure. None of the animals drinking distilled water developed frank hypertension, although one had attained a pressure of 150 mm Hg by the last reading. This rat had by far the largest heart and kidney of its group. Hypertension had appeared in the saline group by the 21st day when one animal had a pressure of 164 mm Hg. A week

later half the animals were hypertensive, an incidence which finally reached 60%. Not until the 4th week did a significant difference in average pressures between groups on saline and those on water ($P<.05$) develop.

By contrast, there was a 30% incidence of hypertension in the sucrose-saline group by the 14th day and 4 other animals were in the 140-149 mm Hg pre-hypertensive range. Although none of the glucose-saline group had pressures above 150 mm Hg at this time, 5 were in the pre-hypertensive range. In the third week 90% of the former group and 60% of the latter were hypertensive. At the last reading the respective incidences were 100% and 90%. Although none of the hypertensives on saline developed pressures above 190 mm Hg, 5 in the sucrose-saline and 4 in the glucose-saline groups had pressures ranging from 192 mm Hg to 265 mm Hg. There was a significant difference between the group average systolic pressure of rats drinking either of the sugar-saline solutions and those drinking either saline or water at each of the periods from the 14th day onward ($P<.01$ or more). Only on the 14th day was there a difference between the pressures of the 2 sugar-saline groups ($P<.05$). The response is shown in Fig. 1.

Organ Weights. Cardiac weight was significantly greater in rats drinking each of the solutions containing salt ($P<.01$ or more) than in those drinking water. The effect was most marked when the solutions contained either sugar, correlating well with the greater incidence and severity of hypertension. The hearts of the two groups drinking sugar-saline solution did not differ significantly from each other, but were in each case larger than in rats drinking only saline ($P<.05$).

Kidney weight was increased in rats drinking either saline or sucrose-saline ($P<.05$ or more) as compared with water controls, but curiously was not in rats drinking glucose-saline.

Adrenal gland weight in rats drinking saline averaged slightly less than in rats drinking water; and the glands of rats drinking sugar-saline solutions were smaller still. Only the glands of rats drinking sucrose-saline proved to be statistically smaller ($P<.05$) than those of controls. There was no evidence of thymus involution in any of the groups (Table I).

Vascular Lesions. The single animal in the water group with an enlarged kidney and a terminal pressure of 150 mm Hg was found to have several severely hyalinized glomeruli in the kidney, and foci of tubular atrophy; some tubules contained hyaline casts. Both heart and pancreas were free of pathologic changes, as were all organs of the remaining rats. Of the group on saline, 6 had glomerular hyaline changes, 2 with moderate and 4 with slight severity. Neither cardiac nor pancreatic lesions were seen. Eight of the rats on sucrose-saline had hyalinized glomeruli, 3 to a moderately severe degree. Two of these, with terminal pressures of 265 mm Hg and 210 mm Hg, also had areas of myocardial necrosis and sclerosis of coronary arteries, and polyarteritis of pancreatic vessels. Four rats on glucose-saline had glomerular hyalinization, one moderately severely and 3 showing mild changes. Two of these, with terminal pressures of 192 mm Hg and 234 mm Hg, also had areas of cardiac necrosis, but none had pancreatic lesions (Table II).

Discussion. The hexose monosaccharide glucose, and the glucose-fructose disaccharide, sucrose, proved equally efficacious in promoting saline consumption despite the greater sweetness of the latter. The result was that whereas the intake of water and saline failed to increase as rapidly as the growth rate, the intake of sugar-saline solution increased more rapidly. Under these circumstances it is not surprising that the sugars increased the incidence and severity of hypertension to substantially the same degree, and that from the second week onward the average arterial pressure of either sugar-saline group was significantly greater at each of the intervals than in either of the two other groups. Unpublished studies have shown that the non-caloric sweeteners, saccharine and cyclohexylsulfamate, have a like effect. In neither instance, however, is the increased intake as great, nor the effect as pronounced, as when sucrose solutions of equal sweetness are used. This presumes of course that rats interpret the respective sweetnesses as would humans.

Since the degree of cardiac hypertrophy

TABLE I. Comparative Effects of Various NaCl Drinking Solutions on Blood Pressure and Organ Weight.

Group	No. rats	Final body wt, g	% Group hyper-tensive	Final avg B.P., mm Hg	Organ wt, mg/100 g body wt			
					Heart	Kidney	Thymus	Adrenal
Distilled water	8	173 ± 4*	12.5	135 ± 3	363 ± 7	830 ± 34	234 ± 15	40.9 ± 1.8
1% NaCl	10	169 ± 3	50	153 ± 7	406 ± 11	982 ± 34	232 ± 10	40.5 ± 1.2
1% NaCl 5% sucrose	10	177 ± 5	100	195 ± 9	485 ± 28	996 ± 62	209 ± 13	36.9 ± .9
1% NaCl 5% glucose	10	176 ± 2	90	183 ± 9	463 ± 24	842 ± 24	223 ± 10	38.3 ± 1.2

* Mean ± S.E.M. Underlined figures differ significantly from controls. "t" test ($P < .05$).

in hypertensive animals depends upon the duration and magnitude of blood pressure elevation, it was to be expected that heart weight of rats drinking sugar-saline would exceed that of rats drinking saline, which in turn would be greater than in rats drinking water. Such was the case. Cardiac vascular lesions however were found only, although not always, in rats with arterial systolic pressures above 190 mm Hg and were thus confined to sugar-saline groups.

In general, the degree of renal enlargement in rats with salt hypertension correlates well with the severity of the condition, but such was not uniformly the case in this instance. Although there was good agreement within a given group there were occasional exceptions, and many hypertensive rats in the glucose-saline group with severe hypertension had smaller kidneys than did many of the normotensive rats in the saline group, on either an absolute or a relative basis. There is no obvious explanation for this since the former were more hypertensive and consumed more salt than the latter. Renal lesions were substantially milder in the glucose-saline animals, than in those of the other two groups on a high salt intake, which doubtless accounted for the lesser kidney weight. It is difficult to hold salt culpable for the single instance of mild hypertension, severe glomerulosclerosis and cardiac hypertrophy in the group given water to drink. This is best ascribed to a spontaneous primary renovascular disease of unknown etiology.

The interaction between carbohydrate and saline in the genesis of hypertension and vascular lesions is complex. Since the sugars increased the level of salt intake they accelerated the rate at which hypertension developed and exacerbated. Under these circumstances cardiac hypertrophy and cardiac damage were enhanced. The effect upon the kidney was not as straightforward. Increased salt ingestion and severe hypertension undoubtedly favor increased renal damage. This is the effect obtained in long-term studies, and under most circumstances where the carbohydrate causes increased saline consumption(5,6). On the other hand when sugars are given to animals under circumstances where saline ingestion is not increased, which occurs in rats given aldosterone and saline(11), desoxycorticosterone and saline(12,13) or sucrose in 10% concentration in saline(8), the carbohydrates appear to reduce the severity of lesions. The present results suggest that this may also be true of short-term experiments with 5% glucose 1% saline, although not with sucrose-saline. Why glucose should have a greater protective effect than sucrose, whether it would also be exhibited in long-term studies where the cumulative effects of salt would be expected to be determinative, and whether it can be consistently demonstrated to prevail

TABLE II. Percentage Incidence of Hypertension and Vascular Lesions as Related to Fluid Consumed.

	Hyper-tension	Renal lesions	Cardiac lesions	Poly-arteritis
H_2O	12.5	12.5	0	0
NaCl	60	60	0	0
Sucrose + NaCl	100	80	20	20
Glucose + NaCl	90	40	20	0

under varying experimental circumstances, are questions that are being examined.

The adrenal response is analogous to that of the kidney. Increased salt ingestion causes greater suppression of the adrenal glomerulosa, and it is even possible that the high level of carbohydrate decreases the demand for glucocorticoid, thus contributing to reduced adrenal weight. On the other hand the stress imposed by hypertensive vascular disease favors adrenal enlargement. The usual result of these operations is that the average group adrenal weight is depressed(5,6,11,12), but not always to a significant degree, partly because of glandular enlargement in some severely hypertensive rats, and also because the glomerulosa, to which the atrophy is principally confined, contributes relatively little to adrenal mass.

Summary. The quantity of 1% saline consumed and the development of salt hypertension in rats were comparably enhanced by addition of either glucose or sucrose in 5% concentration to the drinking solution. Cardiac hypertrophy and lesions were equivalently increased. A curious, and as yet unexplained finding, is that whereas kidney enlargement accompanied consumption of either saline or sucrose-saline solution, such was not the case with glucose-saline. Here the kidney weight did not exceed that of controls, and renovascular lesions although present were less pronounced than when other saline solutions were drunk.

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Intestinal Metabolism of Cholesterol: Evidence Against Side-Chain Oxidation by Mammalian Intestinal Mucosa.* (31492)

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The intestinal mucosa carries out several functions which are critical to the sterol economy of the mammal. Not only does this tissue absorb both dietary sterol and biliary sterol undergoing enterohepatic circulation (1), but also it delivers sterol to the intestinal lumen for fecal excretion(2). Moreover, the mucosa synthesizes sterols(3,4), and recent studies have shown that cholesterol of intestinal origin may account for a significant portion of the total circulating cholesterol(5).

It is apparent from the above that the sterol content of the intestinal mucosa itself represents a balance between additions, including sterol absorbed or synthesized, and losses, including sterol delivered to the gut lumen or to the peripheral circulation. It has not been established, however, that these known routes of loss are adequate to account for the disposition of the absorbed and locally synthesized sterol. Therefore, the possibility exists that there are additional pathways by

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