

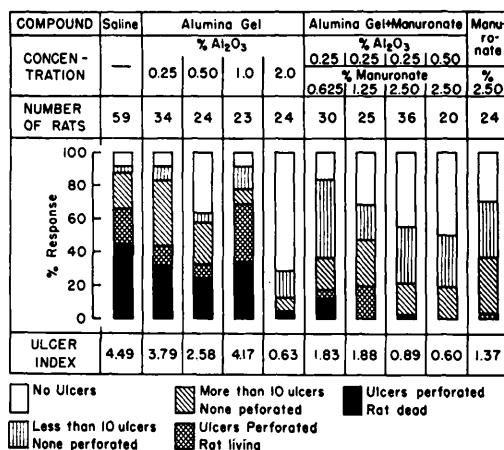


FIG. 1. Effect of alumina gel and Manuronate on incidence of ulcers in the Shay rat.

centrations of 0.625 and 1.25%, both greatly reduced ulcer incidence, the 2 showing approximately equal potency. An increase of sodium polyanhydromannuronic acid to 2.5% in 0.25% Al₂O₃ further decreased ulcer formation. Sodium polyanhydromannuronic acid sulfate, 2.5% in 0.5% alumina gel reduced ulcer formation still more.

A 2.5% solution of sodium polyanhydro-

mannuronic acid sulfate without alumina gel, also reduced ulcer formation, the efficacy being approximately mid-way between 1.25 and 2.50% sodium polyanhydromannuronic acid sulfate in 0.25% alumina gel.

Summary. 1) A study has been made of the effects of sodium polyanhydromannuronic acid sulfate, alumina gel, and mixtures of the two, on incidence of ulcers in the Shay rat. 2) Each provided significant protection from ulcers and mixtures of the two reduced ulcer formation to a greater degree than either alone.

We wish to thank Mrs. Margot Gruenstein and Dr. Harry Shay for their advice concerning the method used.

1. Babkin, B. P., and Komarov, S. A., *J. Canad. M. A.*, 1932, v27, 463.
2. Zaus, E. A., and Fosdick, L. S., *Am. J. Digest. Dis. Nutr.*, 1934-35, v1, 177.
3. Levey, S., and Sheinfeld, S., *Gastroenterology*, 1954, v27, 625.
4. Shay, H., Komarov, S. A., Fels, S. S., Meranze, D., Gruenstein, M., and Siple, H., *ibid.*, 1945, v5, 43.

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Relation of Sodium, Potassium, and Chloride Intake to Cortisone Action During Food Restriction. (22503)

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In a recent study(1), it was reported that the increase in renal size noted in rats on potassium low diets containing NaCl is not observed if the NaCl is replaced by NaHCO₃. It seemed desirable to extend these studies to include observations of food and water intake and to investigate the relation of cortisone to these functions on account of its importance for salt excretion. As on previous occasions, it seemed expedient to carry out the studies on rats whose weights were kept constant by restricted feeding.

Materials and methods. Male albino rats weighing approximately 100 g were kept individually in cages with wire bottoms and were provided with bottles suitable for the determination of water intake. They were weighed daily and supplied with enough food to keep their weight constant within ± 2 g. The requirements were eventually calculated as calories per gram body weight per week. Details of the procedures will be reported elsewhere(2). The basic experimental diet consisted of 30% test casein, 10% commer-

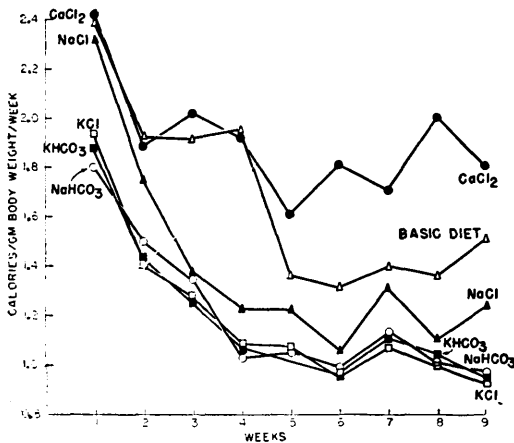


FIG. 1. Influence of various salt supplements on caloric requirements for weight maintenance, each point representing average for 8 male rats of about 100 g.

cial lard, 54% dextrose, 2% cellulose, liberal amounts of all vitamins,* and approximately 4% of a salt mixture containing the essential minerals except Na, K, and Cl. We estimate from the K and Na values known for test casein that the daily intake of the animals on the basic diet was about .2 mg of Na and 1 mg K.[†] The Cl intake may have amounted to 3 mg. When desired, this basic diet was supplemented with .92% NaCl, or equivalent amounts of NaHCO₃, KCl, or KHCO₃. Half equivalent amounts of CaCl₂ or NH₄Cl were used because animals fed these salts required roughly twice as much food for weight maintenance as those on the Na and K containing diets. Cortisone was fed in concentrations of 25 - 50 mg cortisone acetate per kilo of diet, which permitted a daily intake of .25 - .50 mg. In one experimental series, .5 mg cortisone acetate was injected subcutaneously in .1 cc of sesame oil 6 times weekly.

Results. In Fig. 1 are shown average caloric requirements for weight maintenance of

* We are indebted to Dr. Leo Pirk, Hoffmann-La Roche, Nutley, N. J., who generously supplied us with most of the synthetic vitamins used. Vitamins were also received from Barnett Laboratories, Long Beach, Calif., Merck and Co., Rahway, N. J., and the Sterling-Winthrop Research Institute, Rensselaer, N. Y.

[†] This was concluded from data kindly supplied by General Biochemicals, Chagrin Falls, O.

groups on experimental diets with indicated salt supplements. Caloric requirements for weight maintenance of rats on a restricted intake of a "normal" diet decline sharply during the first 4 or 5 weeks and remain fairly constant thereafter(3). As can be seen from the figure, similar curves were obtained with all experimental diets. The decline was least pronounced for animals receiving CaCl₂, whose requirements were eventually twice as high as those of rats given Na or K salts. This finding was confirmed in 3 additional experiments. In 2 experiments with NH₄Cl, similarly high intakes were found. With the unsupplemented diet, food intake was usually not so high as with CaCl₂ or NH₄Cl but was much higher than with Na or K supplements. The caloric requirements of animals receiving NaHCO₃, KHCO₃, KCl, or a complete diet

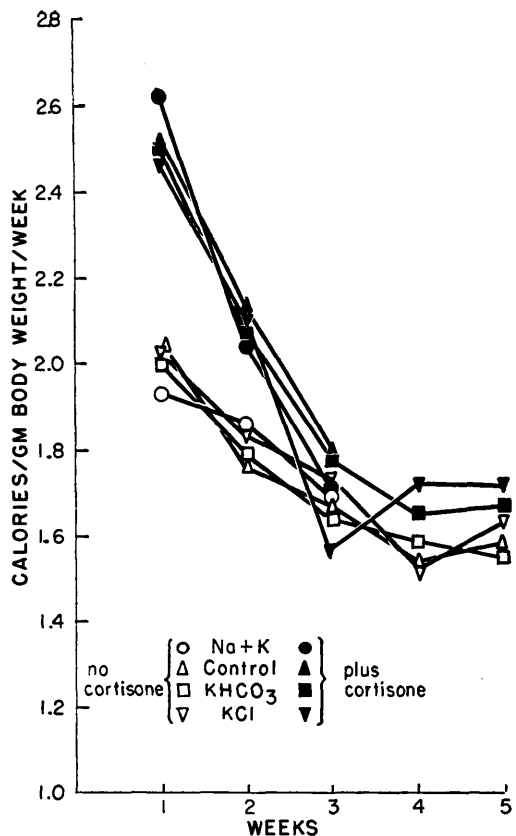


FIG. 2. Influence of cortisone acetate and K salt supplements on caloric requirements for weight maintenance, each point representing average for 8 male rats of 100 g. "Control" refers to group on complete diet.

differed little from one another. In the experiment recorded in Fig. 1, requirements for the NaCl-containing diet were somewhat elevated, but this was true only 4 times in 8 series.

In another series similar to those just described, cortisone acetate was added to the diet. Fig. 2 shows that the initial caloric requirements of animals fed K salts and cortisone were much higher than those of animals given no cortisone. When animals on cortisone are permitted to eat freely, their food utilization is depressed(4). But, as Fig. 2 shows, low utilization (as reflected in high requirements) was observed only initially. The requirements decreased rapidly and eventually hardly differed from those of controls.

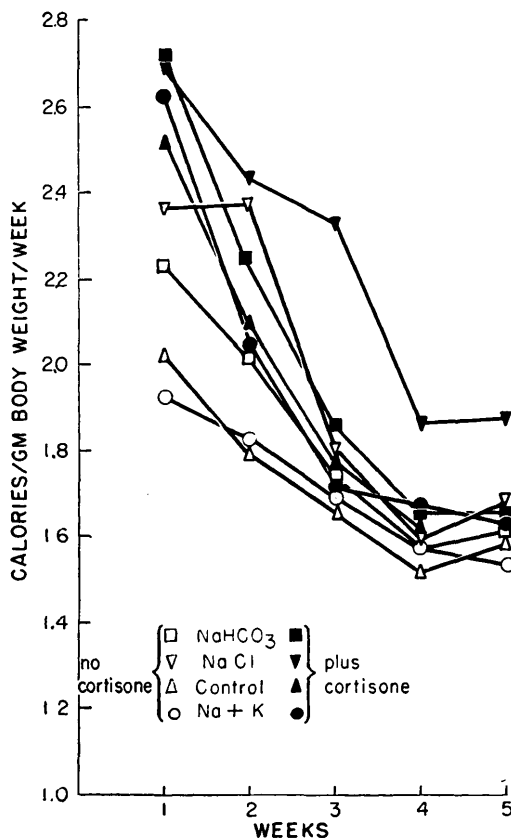


FIG. 3. Influence of cortisone acetate and Na salt supplements on caloric requirements for weight maintenance, each point representing average for 8 male rats of 100 g. "Control" refers to group on complete diet.

In Fig. 3 are given the results of feeding Na supplements. In general, the animals behaved like those with K supplements, the requirements of the cortisone groups being initially higher than those of their controls but declining to the same level. Only the animals receiving NaCl and cortisone ran persistently higher than all of the other groups, the differences being statistically significant in all 4 series.

With NH_4Cl supplements, requirements were just as high as with CaCl_2 (Fig. 1). Addition of cortisone to either the basic diet or that containing NH_4Cl made no difference; but when cortisone was fed along with CaCl_2 , requirements were mildly yet significantly reduced in the 2 series carried out. Thus, cortisone had opposite actions in CaCl_2 and NaCl supplementations.

Fig. 4 gives the weekly individual water intakes. With CaCl_2 , the consumption was 4 times as high as that of the controls on the complete diet. Addition of cortisone reduced the intake. The difference between the groups with and without cortisone was just on the borderline of statistical significance in this series but more pronounced in a second experiment. With NaCl, the water intake was initially twice as high as that of the controls on the complete diet but declined sharply. In two separate series with cortisone and NaCl, the intakes were eventually much higher than without cortisone.

Fig. 5 gives a log-log plot of the kidney weight against the body weight of animals kept on restricted food intake and given the various salt supplements with and without cortisone. The diagonal lines delimit the maximum spread for animals freely eating the complete diet. The renal weights of the controls and of the animals receiving KCl or KHCO_3 were within normal limits; administration of cortisone made no difference. With CaCl_2 , the kidneys were twice as heavy as normal; addition of cortisone made for somewhat lower kidney weights in 2 experimental series. With NaCl supplements, kidneys were markedly heavier, as has been observed previously(5), and cortisone increased the weights further. In contrast, the kidney

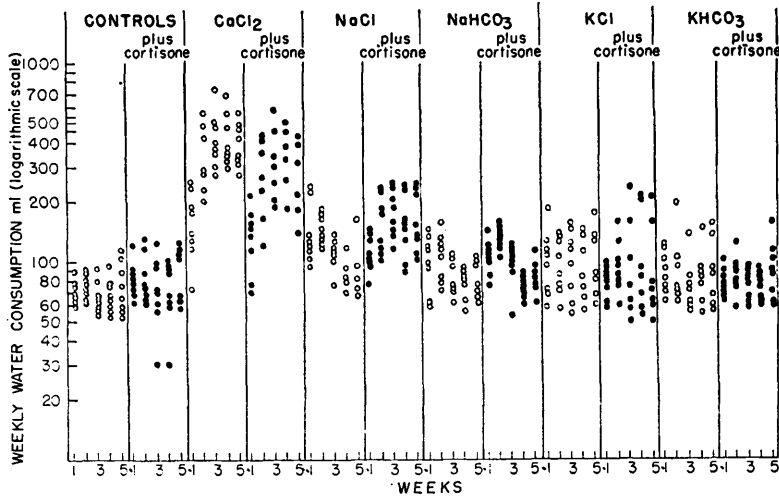


FIG. 4. Influence of cortisone acetate and various salt supplements on thirst, each point indicating weekly intake of one male rat of about 100 g kept at constant weight. "Control" refers to rats on a complete diet.

weights of rats fed NaHCO₃ were on the upper limit of the normal; cortisone led to mild increases.

The circumstance that cortisone exerts opposite effects on the kidney with NaCl and CaCl₂ is remarkable inasmuch as the histological lesions associated with the 2 supplements are identical.[‡] This may deserve clinical consideration in the treatment of nephrosis.

When the relation of the adrenal weight to the body weight was studied, it became evident that, on the average, the adrenals were heaviest with NaCl and lightest with K salts. Cortisone and NaCl sometimes led to development of extremely heavy adrenals. With NaHCO₃, adrenals scarcely differed from those of controls on complete diet, and cortisone made no difference. With the basic diet or that supplemented with CaCl₂, adrenals were heavier than those of controls; cortisone reduced their size.

The liver weights of animals fed K salts without Na were lower than those of animals freely eating a complete diet. Cortisone was without effect. With NaHCO₃, livers were a little heavier and cortisone increased their weight slightly. With NaCl, livers differed

little from those of the bicarbonate group, but cortisone substantially increased their size (after 6 weeks of food restriction, from roughly 3 to over 4 g in animals weighing about 100 g).

The thymic weights were reduced, as was to be expected; and various salts seemed to make no difference. The testicular weights were not remarkable.

Injections of cortisone did not change the results materially. It seemed, however, that the decline of caloric requirement for weight maintenance was, in the injected group, not quite so rapid as in the group given cortisone

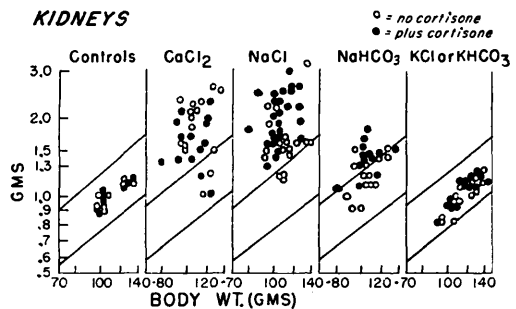


FIG. 5. Influence of cortisone acetate and various salt supplements on the kidney-body wt relation (log-log scale), each point representing one male rat of about 100 g kept at constant weight for about 6 wk. Diagonal lines delimit the spread for male rats freely eating a complete diet. "Controls" were kept at constant weight on the complete diet.

[‡] The histological studies were carried out in co-operation with Dr. Herbert Stoerk of the Merck Institute for Therapeutic Research, Rahway, N. J.

in the diet. This was probably so because dietary cortisone intake of the latter animals declined as they ate less, whereas the daily dose of cortisone for injected animals remained constant.

Summary. 1. Caloric requirements, water intake, and organ weights were determined for rats whose weights had been kept constant by restricted feeding of diets low in Na, K, and Cl with and without cortisone acetate. 2. Whereas ordinarily requirements for weight maintenance decline sharply during the first 5 weeks and become constant thereafter, little if any decrease was noted without Na and K salts. With cortisone, requirements for all diets except those containing CaCl_2 or NH_4Cl were initially much higher than without cortisone but went down rapidly. However, with NaCl and cortisone, the requirements were higher than with K salts or NaHCO_3 and cortisone. On CaCl_2 , the requirements were reduced by cortisone. 3. The water intake

of animals receiving neither Na nor K was very high. Cortisone reduced the intake of the CaCl_2 -supplemented rats. The opposite effect was noted with NaCl. 4. Organ weight determination reaffirmed that the increase in kidney weight noticed on NaCl-containing, K salt-low diets could be avoided by replacement of NaCl by NaHCO_3 . The renal changes were therefore not the consequence of simple K deficiency. Cortisone enhanced renal enlargement in animals on K salt-low, NaCl-containing diets. 5. Cortisone acetate and NaCl reinforce, under certain conditions, some of each other's actions.

1. Kaunitz, H., *Laboratory Invest.*, 1956, v5, 132.
2. Kaunitz, H., Slanetz, C. A., Johnson, R. E., and Guilmain, J., *J. Nutrition*, in press.
3. Quimby, F. H., *ibid.*, 1948, v36, 177.
4. Winter, C. A., Silber, R. H., and Stoerk, H. C., *Endocrinology*, 1950, v47, 60.
5. Meyer, J. H., *J. Nutrition*, 1954, v52, 137.

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Blood Gases in Cholera Patients and in Normal Subjects. (22504)

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Acute purging and vomiting in cholera produce marked reduction in plasma volume with concomitant increase in cell volume. This hemoconcentration affects the hemodynamics of circulation leading to alteration in the normal physiology of blood circulation. The only form of therapy which has stood the test of time as postulated by Rogers(1) is administration of solutions of sodium chloride to maintain the normal physiology of circulation. This form of treatment has been effective in many cases though some die in spite of the treatment, due to kidney failure, resulting in uremia. A reduction in alkalinity of blood was also reported(1,2). The cause of death in cholera is not definitely known. It might be due to acidosis. It might also be due to inadequate supply of oxygen to the

tissues. In the present study, therefore, oxygen and carbon dioxide contents of the whole blood and the bicarbonate content of plasma in patients suffering from cholera and in normal persons were compared.

Methods. Patients admitted into the Nilratan Sircar Medical College Hospitals, Calcutta, with typical symptoms of cholera namely passage of rice-water stool, vomiting and collapse were selected. As a routine procedure stool was cultured and the cases whose stool showed the presence of cholera vibrio were included in the present report. Upon admission and before any treatment was rendered, blood was drawn from the antecubital vein with a dry syringe and delivered in a centrifuge tube under liquid paraffin. The tube was constricted in the middle forming a nar-