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Effect of a High Salt Diet on Survival of Adrenalectomized Rats.

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(Introduced by W. W. Swingle.)

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That NaCl is beneficial in the treatment of experimental adrenal insufficiency was established by the earlier work of Stewart and Rogoff,[1] Banting and Gairns,[2] Marine and Baumann,[3] and Corey;[4] and the recent work of Loeb *et al*,[5, 6] Harrop *et al*,[7] Swingle *et al*,[8] Zwemer,[9] and Rubin and Krick.[10]

A consensus of the findings is that NaCl feeding in dogs and cats will prolong, but not indefinitely maintain, life after total adrenal ablation. Rubin and Krick found, however, that in 8 rats a drinking solution of 0.0329% $CaCl_2$, 0.015% MgCl, 0.07% NaCl and 0.035% KCl given upon the appearance of adrenal insufficiency symptoms, would maintain life for 4 months or more in animals which normally would not live longer than 10 days. At the time of their publication these authors had apparently not determined, by discontinuing treatment, whether accessory adrenals had assumed a functional condition. From their work it would appear that the rat, unlike the cat and dog, will live indefinitely if fed a high salt diet after adrenalectomy. At the time of Rubin and Krick's publication we were studying the effects of adding salt to the diets of adrenalectomized rats. In addition to this we adopted their technique of adding salt to the drinking water, a method probably more effective.

In previous experience with our rat colony we found that ap-

1 Rogoff, J. M., and Stewart, G. N., *Am. J. Phys.*, 1928, **84**, 649.

2 Banting, F. G., and Gairns, S., *Am. J. Phys.*, 1926, **77**, 100.

3 Marine, D., and Baumann, E. J., *Am. J. Phys.*, 1927, **81**, 86.

4 Corey, E. L., *Am. J. Phys.*, 1927, **79**, 633.

5 Loeb, R. F., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 808.

6 Loeb, R. F., Atchley, D. W., Benedict, E. M., and Leland, J. J., *J. Exp. Med.*, 1933, **57**, 775.

7 Harrop, G. A., Soffer, L. J., Ellsworth, R., and Trescher, J. H., *J. Exp. Med.*, 1933, **58**, 17.

8 Swingle, W. W., Pfiffner, J. J., Vars, H. M., and Parkins, W. M., *Am. J. Phys.*, 1934, **108**, 159.

9 Zwemer, R. L., *Endocrinology*, 1934, **18**, 161.

10 Rubin, M. I., and Krick, E. T., PROC. SOC. EXP. BIOL. AND MED., 1933, **31**, 228.

proximately 95% do not survive adrenalectomy.[11] In the latest adult control series 4 out of 24 survived longer than 30 days, 2 longer than 50 days.

In the present experiments, 1.5% NaCl was added to the stock diet* in part of the cases, 2.5% in the others. Either the Rubin-Krick salt solution or 0.9% NaCl solution was given the animals to drink. As far as we could tell one of these feeding-drinking combinations was no more effective than another, so further distinctions between them are not made here.

Twenty-three young, but mature, adrenalectomized rats, weighing from 140 to 200 gm., were studied. The salt treatment was continued for 30 days after adrenalectomy, at which time distilled water and the stock diet were substituted. The results of this treatment from the standpoint of survival can be conveniently divided into 3 categories:

1. Five cases, unlike those of Rubin and Krick, succumbed from 14 to 25 days after operation, *i. e.*, during the course of treatment. with typical symptoms of adrenal insufficiency.

2. Six animals survived and gained weight during the course of the treatment, were apparently in good condition when the treatment was stopped, but after being returned to normal diet developed adrenal insufficiency and died in 10 to 15 days.

3. Twelve animals, approximately 50%, survived in good condition while treated, and after treatment was discontinued gained weight and remained in apparently normal health until killed for autopsy 8 or more weeks after operation. In 7 of these animals accessory adrenals were found.

The survival of 50% after treatment was discontinued is similar to the results we obtained in this colony after withdrawing cortical hormone treatment.[12] Thus it would appear that any agent that will delay the appearance of adrenal insufficiency will, probably by allowing time for the hypertrophy of accessories, cause indefinite survival in this colony in about 50% of the cases.†

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[11] Gaunt, R., *Am. J. Phys.*, 1933, **103**, 494.

*Our stock diet is composed of 9 parts by weight of GLF Calf Meal, and one part ground meat and bone scrap. To this is added yeast, cod liver oil, and lettuce.

[12] Gaunt, R., and Gaunt, J. H., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 490.

†Since these experiments were completed we have carried out a series of similar studies using animals operated at 30 days of age. This latter work is sufficiently complete to indicate that the results obtained are similar to those reported above for adults, although the total fatalities are considerably greater.

Of 46 untreated controls only 2 (4.4%) survived for as long as 2 months and

Twelve out of 14 attempts to revive animals in the late stages of adrenal insufficiency, either by intraperitoneal normal saline injections or by feeding normal saline or the Rubin-Krick salt solution were unsuccessful. In 2 cases revival was effected. These revivals were not attempted until a fall in body temperature indicated severe adrenal insufficiency, although the animals could in all probability in every case have been revived with cortical extract.

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Improved Colorimetric Method for Determination of Bromide Concentration in Blood and Cerebrospinal Fluid.

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In our previous study[1] dealing with determinations of bromide in blood and in cerebrospinal fluid it was pointed out that with the colorimetric procedure of Hauptmann[2] one cannot recover the actual amount of bromide in blood serum. According to Wuth's assumption the precipitates of blood proteins retain a certain amount of bromide.[3] However, with another method[4] for the bromide determination in which, like Wuth, we also used protein-free filtrates, we were always able to recover the total amount of bromide dissolved in various specimens of blood serum.

Having inferred from these findings that proteins are not essentially responsible for the loss of bromide, we tried out *in vitro* the effect of various blood components on the bromide determination: Dissolving, respectively, uric acid, creatinine, urea, glucose, amino-acids (glycine), lactic acid, potassium sulfate, sodium carbonate, magnesium-ammonium phosphate, potassium iodide and sodium

these when killed for autopsy showed large accessories. Forty-four (95.6%) died within 34 days; the average survival was 8 days.

In 41 animals given salt treatment for 30 days after operation, only 18 (43.9%) died during the course of treatment, the average survival being 9 days. Twenty-three animals (56.1%) were alive when the treatment was discontinued. At this writing the survival of this group, after treatment was stopped, has not been determined.

1 Katzenelbogen, S., and Goldsmith, H., *Am. J. Psych.*, 1931, **10**, 1045.

2 Hauptmann, A., *Klin. Wochnschr.*, 1925, **4**, 1629.

3 Wuth, O., *J. A. M. A.*, 1927, **88**, 2013.

4 Hastings, A. B., and van Dyke, H. B., *J. Biol. Chem.*, 1931, **92**, 24.