TABLE I.
Serological Comparison of Products Formed from Sucrose by Sterile Enzyme Solutions with Products Formed in Living Cultures.

Strain of leuconostoc	Reactivity *vs.* types 2, 20 and 12 antipneumococcus serums			
	Enzyme-sucrose mixtures incubated 5 days at 23°C		Supernatant fluids of sucrose broth cultures	
	2 and 20	12	2 and 20	12
B	++++	+	++++	+
M	+++	0	++++	+
O	++++	+	++++	+
A	+++	+++	+++	+++
C	++++	++++	++++	++++
K	+++	+++	++++	++++

++++, precipitation with 1:5000 or 1:10000 dilution of the antigens.
+++, " " 1:500 or 1:1000 " " " "
+, " " 1:10 or 1:20 " " " "
0, no precipitation with 1:10 " " " "

enzyme-sucrose mixtures of strains *B, M* and *O,* like the culture fluids of those strains, had only slight capacity to react with type 12 in comparison to their capacity to react with types 2 and 20 antipneumococcus serum; whereas the enzyme-sucrose mixtures of strains *A, C* and *K,* like the culture fluids of those particular strains, had as high capacity to react with the type 12 as with the types 2 and 20 antiserums.

It is important to note that this comparison, based on the *ratio* of reactivities with 3 different antiserums, is an unusually critical sort of test which is capable of detecting a minor serological difference even among products which appear alike if tested against a single antiserum. Consequently, the agreement shown in Table I in respect to the *ratio* of reactivities against the 3 types of antipneumococcus serum is an especially significant index of close serological likeness between the materials formed from sucrose by sterile enzymes and the materials formed in living cultures of the strain of leuconostoc bacteria from which the enzyme had been derived.

14285 P

Protection of Normal Rats Against Death from Water Intoxication with Adrenal Cortical Substances.*

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It is well known that, in general, resistance to stress is low in adrenalectomized animals and that protection can be afforded by appropriate replacement therapy. Similarly adrenalectomized animals are susceptible to the intoxicating effects of excess water, and studies have been made on the effects of various steroid substances in repairing this deficiency.[1] Attempts to increase the re-

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1 Eversole, W. J., Gaunt, R., and Kendall, E. C., *Am. J. Physiol.,* 1942, **135,** 378.

TABLE I.
Average Figures Concerning the Effect of Adrenal Cortical Substances on Animals Given Lethal Doses of Water.

Exp. No.	No. animals	Treatment	Water dose, cc	Times water given	% water excreted at following hours: 1st	4th	7th	9th	Rectal Temp. °F at following hours: 1st	4th	7th	9th	Chloride excreted (as mg NaCl)	No. convulsive	No. died
I.	3	9 cc 0.8% NaCl	9.7	11-15	15	56	61			90	86		97.6	3	3
	3	9 cc Cort. Ext.	10.0	15	11	59	69			96	96		98.6	1	0
II.	6	9 cc 0.8% NaCl	10.0	11-19	7	43	55	49	99	91	87	85	113.4	6	6
	6	9 cc Cort. Ext.	10.0	19	8	60	68	73	99	95	93	92	146.8	1	0
III.	6	1.7 cc P-nut oil	9.3	11-18	8	32	40	51	100	92	87	85	67.9	6	6
	6	12 mg DCA	9.2	18*	23	50	56	58	100	94	89	88	97.6	4	1

* One died after the 15th dose of water; the rest received 18 doses.

sistance of intact animals to stress by the use of cortical substances have been generally (*e.g.*),[2,3] although not in all instances (*e.g.*),[4,5] unsuccessful. The experiments reported here show that a striking protection can be afforded normal animals against the intoxicating effects of water by either a whole extract of the adrenal cortex or desoxycorticosterone acetate (DCA).

Methods. Routine procedures were similar to those previously used.[1] Male rats, fasted 18 hours and weighing approximately 200 g were used. Distilled water (3 cc per 100 sq cm of body surface) was given by stomach tube at half-hour intervals until all of the controls in each of the 3 experimental groups were dead. In the treated animals, 1 cc of cortical extract was given per hour, beginning just before the first dose of water. Controls received 0.8% NaCl similarly. In the DCA-treated series, 5 mg was given subcutaneously 18 hours before the experiment, 5 mg intramuscularly one-half hour before water was started, and 2 mg intraperitoneally during the experiment. Controls received peanut oil in amounts equal to that used as a solvent for the DCA. Experiments on both treated and control animals in each group were run simultaneously. The cortical extract used was a concentrated preparation in which 1 cc represented 200 g of whole gland.

Results. The results are shown in Table I. Two experiments were conducted with cortical extract. The controls were killed by 11 to 15 doses of water in one case, and 11 to 19 in the other. All treated animals received the highest dose of water given to any one of the controls, and all survived. The treated animals also surpassed their controls by the other criteria observed, *i.e.*, maintenance of body temperature, rate of diuresis, and freedom from the typical convulsions of water intoxication. It is well known that saline itself is helpful in preventing water intoxication,[6] so that the comparison here was between two beneficial agents.

DCA was also beneficial, but did not maintain the animals as well, relative to their controls, as did the cortical extract. One DCA-treated animal died before all the controls were dead, and 3 others were greatly weakened and convulsive. The latter 3, however, survived and appeared normal the following day. Since standards by which to establish comparable dosage and methods of administration of the extract and DCA as used here are lacking, the inferiority of the latter in this experiment should not be emphasized. It is, however, consistent with the better results obtained by extract or 17-

[2] Huizenga, K. A., Broffman, B. L., and Wiggers, C. J., *J. Pharm. and Exp. Ther.*, 1943, **78**, 139.

[3] Swingle, W. W., Overman, R. R., Remington, J. W., Kleinberg, W., and Eversole, W. J., *Am. J. Physiol.*, in press.

[4] Selye, H., Dosne, C., Bassett, L., and Whittaker, J., *Canad. Med. Assn. J.*, 1940, **43**, 1.

[5] Katz, L. N., Killian, S. T., Asher, R., and Perlow, S., *Am. J. Physiol.*, 1942, **137**, 79.

[6] Rowntree, L. G., *J. Pharm. and Exp. Ther.*, 1926, **29**, 135.

hydroxy-11-dehydrocorticosterone as compared to DCA in adrenalectomized animals given large doses of water.[1]

The chloride excretion figures are not to be interpreted as measures of renal activity, since the urine samples were contaminated with diarrheal fluid, particularly in the controls. There is a loss of considerable fluid through the intestine in terminal stages apparently due to an eventual failure of water absorption from the intestine.[7] The chloride figures are quoted to show, however, that the protective action of the cortical substances is not through a prevention of the loss of this ion from the body.

While a more detailed study of the action of cortical steroids in the response to excess water will be reported elsewhere, it is perhaps noteworthy that most types of stress in which cortical substances have been given intact animals without consistent success have been shock-producing stimuli, associated with marked hypotension. Water intoxication is a different type of phenomenon in that blood pressure is well maintained until near the time of death.[6,7,8]

Summary. Large doses of adrenal cortical extract or desoxycorticosterone acetate will protect normal rats from doses of water which otherwise produce lethal water intoxication.

[7] Gaunt, R., unpublished observations.

[8] Swingle, W. W., Parkins, W. M., Taylor, A. R., and Hays, H. W., *Am. J. Physiol.*, 1937, **119**, 557.

14286 P

Hair Loss in Male Dogs Fed Stilbestrol.

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Failure of regeneration and loss of hair have been reported[1] in dogs given estradiol benzoate. No account has been found of the same phenomenon in dogs which received synthetic estrogens.

In a recent experiment* 4 male dogs received *by mouth diethylstilbestrol,*† 5 mg tablets, over a period of several months. These animals and 2 other male dogs (serving as controls) were also injected subfascially with methylcholanthrene, the changes resulting from which will be described elsewhere. All of the animals were mongrels about 1½ to 3 years old at the start of the experiment. The weights ranged between 15 and 27 lb. and did not vary significantly.

The first dog received 330 mg of stilbestrol in 20 doses of 5 mg, 19 of 10 mg and 2 of 20 mg in a period of 129 days, at the end of which the hair was missing from the right flank.

The second dog received 1790 mg of stilbestrol in 20 doses of 5 mg and 169 of 10 mg in a period of 292 days, at the end of which the hair was generally thinned, was largely missing from the abdomen and penis, and had failed to regenerate on the forelegs at areas clipped for vein puncture.

The third dog received 1850 mg of stilbestrol in 185 doses of 10 mg in a period of 280 days, at the end of which the hair was missing from the thighs, buttocks, perineum, abdomen, face, and the ventral surface of the tail, thorax, and neck.

The fourth dog received 2985 mg of stilbestrol in 100 doses of 10 mg, 6 of 15 mg, 6 of 20 mg, and 71 of 25 mg in a period of 291 days, at the end of which the hair was absent from the base of the tail, the lumbar regions, the scapular regions, the abdomen,

[1] Gardner, W. U., and DeVita, J., *Yale J. Biol. and Med.*, 1940, **13**, 213.

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