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Effect of Desoxycorticosterone Acetate* upon Blood Sugar and Electrolytes of Adrenalectomized Rats.

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Following the synthesis of desoxycorticosterone by Steiger and Reichstein,¹ it was shown by Thorn, *et al.*,^{2, 3} and Levy-Simpson⁴ that this compound is effective in the treatment of adrenal insufficiency, both in adrenalectomized animals and in patients with Addison's disease. The studies thus far reported have shown that the effects of desoxycorticosterone acetate upon the concentrations of serum sodium and potassium, and upon plasma volume are identical with those of adrenal cortical extracts.

Adrenal cortical extracts as well as crystalline compounds isolated from the adrenal cortex have been shown by Long and Katzin⁵ to increase the carbohydrate stores of fasted normal and hypophysectomized rats. No data concerning the effect of desoxycorticosterone acetate upon carbohydrate metabolism have as yet been reported.

We have studied the blood sugar, non-protein nitrogen, and serum sodium and potassium of adrenalectomized rats treated with desoxycorticosterone. Blood sugar was determined by the Shaffer, Hartman, Somogyi method,⁶ non-protein nitrogen by the Koch and McMeekin method,⁶ serum sodium by the Butler and Tuthill method,⁶ and serum potassium by the method of Harrison and Darrow.⁷

Male rats of approximately 175 g in weight were adrenalectomized

* A solution of desoxycorticosterone acetate in sesame oil, supplied through the courtesy of Dr. Erwin Schwenk of the Schering Corporation, was used in these experiments.

¹ Steiger, M., and Reichstein, T., *Nature*, 1937, **139**, 925.

² Thorn, G. W., Engel, L. L., and Eisenberg, H., *J. Exp. Med.*, 1938, **68**, 161.

³ Thorn, G. W., Howard, R. P., Emerson, K., and Firor, W. M., *Bull. Johns Hopkins Hosp.*, 1939, **64**, 339.

⁴ Levy-Simpson, S., *Lancet*, 1938, **2**, 557.

⁵ Long, C. N. H., and Katzin, B., *Proc. Soc. Exp. Biol. and Med.*, 1938, **38**, 516.

⁶ Peters, J. P., and Van Slyke, D. D., *Quantitative Clinical Chemistry*, Vol. II, Methods, 1932, Baltimore, Williams and Wilkins.

⁷ Harrison, H. E., and Darrow, D. C., *J. Biol. Chem.*, 1937, **121**, 631.

TABLE I.
Blood Sugar and Serum Electrolytes of Adrenalectomized Rats Fasted 48 Hours.

Treatment	No. of rats	mg/100 ml		m.Eq./l	
		Blood sugar	Blood N.P.N.	Serum Na	Serum K
1. Unoperated controls	6	65 \pm 3.3*	44	140.5	5.2
2. Adrenalectomized, untreated	7	48 \pm 4.2	70	130.4	6.6
3. Adrenalectomized, sodium salts	7	38 \pm 5.0	40	128.8	6.2
4. Adrenalectomized, desoxycorticosterone 1.25 mg daily	6	41 \pm 2.6	47	138.0	5.4
5. Adrenalectomized, desoxycorticosterone 2.5 mg daily	9	63 \pm 2.9	44	137.5	4.7

* Mean \pm standard error of the mean.

The significance of the differences between the mean concentrations of blood sugar were tested using Fisher's⁸ Table of t for small samples. The differences between groups 1 and 2, 2 and 5, and 4 and 5 are considered significant.

⁸ Fisher, R. A., *Statistical Methods for Research Workers*, 1932, London, Oliver and Boyd.

and maintained for 5 days on a diet of Purina Fox Chow and sodium chloride and sodium bicarbonate in the drinking water. They were then fasted 48 hours and on each of the 2 days injected subcutaneously with desoxycorticosterone acetate in doses of 1.25 mg or 2.5 mg. One control group of adrenalectomized animals was fasted and given no treatment during the experimental period; a second group was fasted and injected intraperitoneally with a solution of sodium chloride and sodium bicarbonate. A group of fasted unoperated controls was also studied. At the end of the 48-hour period of fasting the animals were anesthetized with nembutal and blood was taken from the abdominal aorta for analysis.

From the results given in Table I it is seen that untreated adrenalectomized rats fasted for 48 hours show a definite decrease in concentration of blood sugar, an increased concentration of blood non-protein nitrogen and serum potassium, and a decreased concentration of serum sodium. Treatment with sodium salts does not influence the blood sugar but prevents the rise in non-protein nitrogen. The treatment, however, was not sufficient to maintain normal concentrations of serum sodium. The injection of 1.25 mg of desoxycorticosterone acetate per day has no effect upon the blood sugar of adrenalectomized rats, although this dose is sufficient to maintain normal concentrations of serum electrolytes and non-protein nitrogen. The concentrations of blood sugar in the adrenalectomized rats are maintained at normal levels by the injection of 2.5 mg of desoxycorticosterone daily.

Conclusions. The injection of adequate amounts of desoxycor-

ticosterone acetate into fasted adrenalectomized rats does prevent the drop in concentration of blood sugar found in untreated adrenalectomized rats. The amount required to maintain the blood sugar is greater than that necessary to maintain normal concentrations of serum electrolytes and non-protein nitrogen.

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Effect of Local Applications on Development of Ultraviolet Tumors.*

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We have previously demonstrated that the rate of tumor production by ultraviolet light varies with the time of irradiation, with the amount of pigment in the skin, and with the character of the diet.^{1, 2} The present study deals with the effect of various substances on the development of U. V. tumors, when applied directly to tissues in which neoplastic changes are occurring.

Three types of materials were used: oils, oxidizing agents, and carcinogenic compounds. Oils were studied because previous work had shown that the production of U. V. tumors was markedly accelerated by the consumption of a high-fat diet (30% Crisco), on which the fur became definitely greasy. The acceleration, therefore, could have been due to either a local or a systemic effect. By painting oil on the ears of irradiated mice on a normal diet the local factor alone could be studied.

The oxidizing agents were studied because of Roffo's emphasis of the importance of cholesterol in tumor production. He has shown that irradiated cholesterol fogs a photographic plate³ and claims that this reaction is analogous to that taking place within the skin, when an animal is exposed to excess amounts of ultraviolet light. Stavely and Bergmann⁴ and Mayneord and Roe⁵ have demonstrated

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¹ Rusch, H. P., and Baumann, C. A., *Am. J. Ca.*, 1939, **35**, 55.

² Baumann, C. A., and Rusch, H. P., *Am. J. Ca.*, 1939, **35**, 213

³ Roffo, A. H., *Am. J. Ca.*, 1933, **17**, 42.

⁴ Stavely, H. E., and Bergmann, W., *Am. J. Ca.*, 1937, **30**, 749.

⁵ Mayneord, W. V., and Roe, E. M. F., *Am. J. Ca.*, 1937, **31**, 476.