

TABLE II.
Comparative Antigenicity Tests Using Mice and Guinea Pigs.

Toxoid	Mice			Guinea pigs		
	Immunization period, weeks	No. of animals tested	% protected	Immunization period, weeks	No. of animals tested	% protected
Stand. A	3	41	95	6	13	92
No. 1	3	38	96	6	8	87
	3	40	93			
No. 2	3	40	95	6	16	75
				6	10	90
No. 3	3	39	92	6	13	92
No. 4	2	69	100	6	12	92
No. 5	2	67	96	6	13	85
No. 6	3	40	77	6	10	40

unknown toxoid is then compared with that of the standard toxoid tested simultaneously. The technic of the test is otherwise the same as described under Procedure I.

Using Procedure I we have compared the degree of resistance attained in mice and guinea pigs and have obtained the data listed in Table II.

Summary. Swiss mice can be used as test animals in place of guinea pigs for the deter-

mination of the antigenic power of tetanus toxoid. The advantage in the use of mice lies in two facts: (1) the immunization period necessary is only 3 weeks instead of the usual 6 weeks; (2) lower cost of mice permits the use of a larger number of animals and animals of greater uniformity than guinea pigs, which contributes to a greater statistical significance and accuracy of the test.

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Activity of Desoxycorticosterone Acetate upon Oral Administration.

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Comparative studies of the activity of desoxycorticosterone acetate upon parenteral and oral administration have been carried out repeatedly. Grollman found 1 mg of this hormone effective both in maintaining life and promoting growth of adrenalectomized rats, regardless of the mode of administration.¹ On the other hand, more re-

cent studies indicated that the effects produced by injection of the hormone were considerably superior to those following oral administration.² A comparison of the technics of oral administration in the earlier and in the later studies indicated a difference which appeared of possible significance. Grollman mixed the hormone with the diet and thus ensured prolonged or almost continuous intake of the hormone. On the other hand, Kuizenga gave the hormone, dissolved

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¹ Grollman, A., *J. Pharm. and Exp. Therap.*, 1939, **67**, 257.

² Kuizenga, M. H., Nelson, J. W., and Cartland, G. G., *Am. J. Physiol.*, 1940, **130**, 298.

TABLE I.

Exp. No.	Type of treatment	Daily dose, mg	No. of rats	20-day survival, %	Wt change (20 days) g	Survival (days)†	
						Avg	Individual
1	Doca, oral Controls	.09-0.8*	4	75	+22	1 rat died 3rd day*	
			6	0	—	6	2,2,2,7,9,15
2	Doca, oral	.35	7	29	+10	13	7,13,13,14,16
	Doca, parenteral	.33	3	67	+25	1 rat died 13th day	
	Controls		4	0	—	3	2,3,4,4

†Of the rats which died during the experimental period.

*During first 3 days hormone given only in drinking water, an average of only 0.09-0.16 mg being consumed daily by each rat; during next five days hormone also mixed with diet, 0.8 mg per day being consumed in average; during the rest of the experimental period the hormone was again given only in drinking water, an average of 0.26 mg being consumed by each rat.

in a small volume of oil, once daily by stomach tube.² It appeared possible that the absorption of the hormone might not be complete under these conditions. Evidence for the fact that the technic of oral administration may play a significant role in determining the availability of a substance has recently been demonstrated by Schoenheimer's studies.³ In the case of desoxycorticosterone, recent studies of the effect of adrenal hormones on liver arginase activity indicated this hormone to be effective when given to hypophysectomized rats in solution in the drinking water.⁴ It thus seemed indicated to reinvestigate in adrenalectomized rats the activity of desoxycorticosterone upon oral administration under physiological conditions, *i.e.*, by mixing the hormone with diet and drinking water.

Female rats were adrenalectomized at the age of 26-28 days.† They received 1% sodium chloride to drink for one week. From the eighth day on, all rats received a salt-free diet and no more salt water to drink. In Experiment 1, they were then divided into 2 groups, one receiving hormone and the other serving as control. The hormone was given in solution in the drinking water (0.0025 or 0.0033%) as well as, from the

fourth to the eighth day, mixed with the diet. In Experiment 2, the operated rats were divided into 3 groups; one received the hormone (in solution in sesame oil twice daily) by subcutaneous injection, another received a similar dose mixed with drinking water (0.0025%) and diet and a third served as control. The hormone intake was determined for groups of 2 or 3 rats and thus represents an average figure. At the end of a 20 day period of treatment, hormone was withdrawn from all rats until death (1 to 9 days). At autopsy the lumbar region of all operated rats was searched for residual or accessory adrenal tissue. Suspicious tissue was fixed and studied histologically.² A few rats (9% of the total) showed weight gains which were far in excess of those of all other operated rats, treated as well as untreated, while no adrenal tissue could be found by binocular inspection at autopsy. These doubtful cases as well as those in which adrenal tissue was found were not included in the table.

Results. Orally administered desoxycorticosterone acetate was found to maintain the life of adrenalectomized rats and enable them to grow. In Experiment 1 (see Table I), as low a dose as 0.09 to 0.16 mg daily led to a survival of 3 out of 4 rats during the first 3 days, while 3 of 6 controls died during this period. The 3 treated rats also survived and continued to grow throughout the rest of the experimental period, during which the daily hormone dosage was raised to 0.8 mg for 5 days and then again reduced to 0.26 mg. In Experiment 2, the daily oral administration of 0.35 mg hormone enabled all rats to sur-

³ Schoenheimer, R., Ratner, S., Rittenberg, D., and Heidelberger, M., *J. Biol. Chem.*, 1942, **144**, 545.

⁴ Fraenkel-Conrat, H., Simpson, M. E., and Evans, H. M., in press.

† The author is indebted to Dr. M. E. Simpson for her cooperation in performing the operations as well as the histological examinations of possible adrenal remnants.

vive the controls, although only 2 of the 7 rats of the treated group survived the entire experimental period. Gains in body weight were also less pronounced in this than in the corresponding group in Experiment 1. Comparison of oral and parenteral administration indicated that the latter was slightly superior. However, the number of completely adrenalectomized animals receiving the hormone by injection was too small to warrant

foregoing quantitative conclusions in this regard (adrenal tissue was found in 3 rats of this group).

Summary. Desoxycorticosterone acetate was found to be beneficial to adrenalectomized rats upon oral administration, *i.e.*, mixed with food and/or drinking water. Dosages of 0.09 to 0.33 mg daily favored survival and growth in such rats on a salt-free diet.

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Partial Maintenance of Adrenal Weight in Hypophysectomized Immature Male Rats by Testosterone Injections.*

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In the course of certain experiments involving the use of hypophysectomized male rats, where routinely it has always been customary to weigh the adrenals, it was noted that after male hormone treatment, the adrenals did not regress to the same degree as did those of litter mate controls. After hypophysectomy, the adrenals always atrophy and lose weight¹ and this observation has been one of the criteria indicating completeness of the operation. Since no mention of a maintenance effect of male hormone on the adrenals of hypophysectomized rats has been made in the literature, a preliminary note on this finding is here presented.

All the rats used in these experiments were from the Long-Evans strain, between the ages of 22 and 35 days at the time of hypophysectomy. There were fed a dry ration of dog and calf meal,² water and a 25% solution of corn syrup *ad libitum*. A part of each litter of hypophysectomized males were injected once daily with .05 cc = 1.25 mg of

testosterone propionate (Peranderen, Ciba)[†] for 10 days, the operated litter mate controls received no injections. At autopsy on the 11th day, the adrenals were removed, carefully trimmed of the surrounding fat and were weighed fresh. Some of the glands were prepared for histological study. Serial sections of all the sellæ turcicae were made and all incompletely operated animals were dis-

TABLE I.
Testosterone Inhibition of the Adrenal Atrophy Which Follows Hypophysectomy.

Exp.	Age	Avg adrenal wt (mg)		% Difference
		Injected	Controls	
I	34	10.4 (4)	8.5 (1)	22
II	35	17.5 (4)	9.5 (2)	84
III	24	11.9 (5)	7.4 (4)	60
IV	25	12.2 (4)	8.0 (1)	53
	22	11.6 (2)	6.4 (2)	81
V*	23	13.4 (3)	6.4 (4)	109

*Total dose of testosterone 6.9 mg in 10 days, all others received 12.5 mg.

Numbers in () indicate number of animals. Results on litters of same age combined.

carded. In all, 8 litters, involving 22 injected and 14 control rats, were used.

A comparison of the average adrenal weights of the injected and control rats within the separate litters is given in Table I, together with the percentage difference of the

*Aided by a grant from the Sackett Research Fund.

¹ Smith, P. E., *Am. J. Anat.*, 1930, **45**, 205.

² Maynard, L. A., *Science*, 1930, **71**, 192.

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