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Effect of Progesterone and Other Hormones on Liver Glycogen.*

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The carbohydrate stores of intact fasting animals can be raised by large doses of cortical hormone.[1, 2] It has recently been shown that progesterone maintains the lives of adrenalectomized animals.[3-9] Since the normal corpora lutea of pseudopregnancy will maintain life after adrenalectomy, this cortin-like activity is probably of physiological significance at least in certain species (references elsewhere[3]).

We report here studies to determine if progesterone and other sex hormones have an action like cortical hormone on carbohydrate metabolism as judged by the effects of acute overdosage on the glycogen stores of fasting animals. We used the ferret in initial experiments because it seems to be in other respects an unusually responsive species to the cortical hormone-like action of progesterone.

In Ferrets. All experimental ferrets were fed for one week prior

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The hormones used here were generously supplied us as follows: Progesterone by Dr. Erwin Schwenk, Schering Corporation; cortical extracts (Eschatin) by Dr. Oliver Kamm, Parke, Davis and Co.; testosterone propionate (Oreton) by Dr. Max Gilbert, Schering Corporation; Stilboestrol and pregnancy urine extract (Follutein) by Dr. J. A. Morrell, E. R. Squibb and Sons; and pregnant mare serum (Gonadin) by Mr. Donald Wonder, Cutter Laboratories.

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to experimentation on weighed and identical portions of Ken-L-Ration, fresh ground meat and fresh milk. Feeding was in such amounts as to permit a weight gain of from 5-10 g per day. All food was withdrawn for the last 24 hours of the experiment. The females were in early but not full estrus if not designated as pseudopregnant. Pseudopregnancy was produced by injections of pregnant mare serum and pregnancy urine extracts. All animals were about 10 months old. Sixty mg of progesterone was given in sesame oil in 5 divided doses beginning 36 hours and ending 8 hours before sacrifice. In the cortical hormone series, 20 cc of cortical extract in sesame oil was given from 36-12 hours before the experiment ended, and 30 cc of aqueous extract was given during the last 12 hours before sacrifice. Controls received sesame oil and saline in amounts similar to the volumes of these solvents used in the cortical extract-treated series. Control and treated cases were run simultaneously.

The results are shown in Table I. It can be seen that both cortical extract and progesterone elevated liver glycogen above the level found in controls while muscle glycogen varied little if any. This was particularly noticeable in pseudopregnant animals which had been under the influence of their own corpora lutea for 2 to 3 weeks

TABLE I.
Ferrets.

Index No.	Sex	Liver Glycogen g %	Liver Glycogen mg % per 100 g body wt	Muscle Glycogen g %
		Controls—Untreated, 24-hour fast.		
25	Male	.330	37.1	.452
26	"	.461	35.6	.463
34	Female	.158	30.0	.380
33	"	.189	28.2	.427
Av.		.285	32.7	.430
		Given 50 cc Cortical Extract, 24-hour fast.		
29	Male	.798	121.0	.594
30	"	.924	125.7	.513
35	Female	.784	156.9	.520
36	"	1.002	195.7	.552
Av.		.877	149.8	.545
		Given 60 mg Progesterone, 24-hour fast.		
27	Male	.781	96.4	.500
28	"	.795	98.2	.551
31	Female	.824	159.0	.468
32	"	.590	100.0	.464
Av.		.748	113.4	.496
		Pseudopregnant—Given 60 mg Progesterone, 24-hour fast.		
20*	Female	1.696	261.0	.546
23	"	0.818	143.5	.621
24	"	1.424	219.1	.545
Av.		1.313	207.9	.571

* Adrenalectomized.

and then given 60 additional mg of progesterone as in other cases. The effect is not through the adrenals as shown by No. 20, an adrenalectomized animal, which had been maintained by her corpora lutea without any cortical hormone for 3 weeks.

Blood sugar figures were generally higher in treated animals. There were indications of increased serum ketones and urine nitrogen after treatment. No significant differences in blood dilution (hematocrit), or serum Na, K, or Cl were found.

In Rats. Experiments were done similarly on 125 g male rats with the exception that a 12-hour fast was used and injections of the sex hormones were begun 48 hours before sacrifice. Cortical hormone was given as follows: 6 cc in oil from 36-12 hours, and 10 cc in hourly divided doses during the last 10 hours before sacrifice.

The liver glycogen and blood-sugar raising effect of cortical hormone as previously reported in rats was confirmed (Table II). If the sex hormones had any effect it was only slight and not significant in this small series. Pending further study these data on rats are presented to show only that the rat does not respond to any of the sex hormones, quantitatively at least, as does the ferret to progesterone.

In a susceptible animal such as the ferret apparently a cortical hormone-like action of progesterone on carbohydrate metabolism can be demonstrated. The possible physiological significance of this fact is being studied further. The weak action of progesterone, if any at all, on this process in the rat may perhaps be correlated with the fact that the rat demands relatively enormous amounts of progesterone for life-maintenance after adrenalectomy, and that progesterone is of no assistance in this species to the stress of water intoxication,[8] muscle work,[10] and lactation[11] following adrenalectomy.

TABLE II.
Male Rats.

	No. rats used	Liver Glycogen g % Mean	Muscle Glycogen g % Mean	Blood Sugar mg % Mean
Controls—Untreated, 12-hr fast	9	0.335	0.441	76.3
Given 16 cc Cortical Extract, 12-hr fast	3	1.061	0.498	119.3
Given 35 mg Progesterone, 12-hr fast	3	0.337	0.457	92.8
Given 50 mg Testosterone Propionate, 12-hr fast	3	0.292	0.429	87.7
Given 35 mg Stilboestrol, 12-hr fast	6	0.443	0.463	96.0

[10] Ingle, D. J., *Proc. Am. Physiol. Soc.*, 1939, p. 127.

[11] Tobin, C. E., personal communication.

Professor C. N. H. Long and collaborators have also been unable to demonstrate an effect of progesterone on the carbohydrate metabolism of rats.[12] Experiments carried out in a different fashion might have given positive results. Gilder and Phillips[13] have found that estradiol-treated rats demonstrated significantly elevated liver glycogens only if glucose-fed.

Summary. Progesterone as well as cortical extract raised the liver glycogen levels of intact fasting ferrets. Pseudopregnancy probably enhanced the effectiveness of progesterone. In a small number of rats cortical extracts had similar effects, while progesterone, testosterone propionate and stilboestrol gave little if any response.

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Hormonal Induction of Abortion.*

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The present experiments represent an attempt to determine whether or not pregnancy may be interrupted in the rabbit by the induction of ovulation during the second trimester of gestation.[1, 2, 3] It was prompted by earlier work[4] upon animals observed during the last trimester of pregnancy in which it had been found that the duration of gestation could be profoundly altered by the induction of ovulation with extract of urine of pregnant women (Antuitrin S). The onset of parturition was delayed long past term in certain animals, while in others labor was induced prematurely. Factors which determined whether pregnancy would be lengthened or shortened were (1) the stage of pregnancy at the time of induction of ovulation, (2) the dosage of pregnancy urine extract adminis-

12 Personal communication.

13 Gilder, H., and Phillips, R. A., *Proc. Am. Physiol. Soc.*, 1939, p. 86.

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