vitamin B_1 concentrates, such as extracts of yeast, rice polish and wheat germ, has enabled us to convert all of the vitamin present into the form by which it may be determined chemically. By difference between the thiamin values obtained before and after hydrolysis, the concentration of the vitamin in the phosphorylated form may be estimated. In the samples assayed we have found some yeast preparations to contain as much as 75% of its thiamin in this form, a rice polish extract 17%, and a wheat germ preparation 10%. Obviously, in the preparation of any dried yeast powder or extract the ratio of phosphorylated to free thiamin in the final product is dependent upon the conditions associated with the preparations. If during the process conditions are such as to allow the phosphatase present to act, a much smaller ratio will be obtained. Our findings of an autohydrolysis of the phosphorylated thiamin in aqueous suspensions of dried yeast powders support the earlier findings of Auhagen[9] that autolyzed yeast loses its cocarboxylase activity.

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Cortical Hormone-Like Action of Progesterone and Non-Effect of Sex Hormones on "Water Intoxication."*

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Gaunt and Hays have shown that crystalline progesterone maintains life and excellent health in adrenalectomized ferrets, whereas the estrogens are toxic and testosterone non-beneficial.[1] These findings probably account for the survival of pseudopregnant adrenalectomized animals.[2] † To determine if other species would respond

[9] Auhagen, E., *Biochem. Z.*, 1933, **258**, 330.

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[1] Gaunt, R., and Hays, H. W., *Science*, in press.

[2] Literature cited by Gaunt, R., and Hays, H. W., *Am. J. Physiol.*, in press.

† Dr. G. W. Thorn reports a confirmation of the life-maintaining action of progesterone in adrenalectomized dogs (personal communication).

similarly, we have tested the effects of progesterone on the life-span of 30-day-old adrenalectomized rats.

Progesterone in oil was given in doses of 1-2 mg per day for 20 days, the dose varying somewhat with the apparent needs of the animal. Untreated littermates were used for controls. Results are shown in Table I. Series I was run during hot summer months (at C.S.H.) and the short survival of controls was due to that fact. Series II was run under our usual, more optimal, conditions for observation of adrenalectomized rats (at W.S.C.). Progesterone pellets implanted under the skin at the base of the ear were not noticeably beneficial. In half of the cases life was maintained as long as progesterone was given, and a definite life-extension was seen in those animals which died on treatment. Equally marked was the greater weight gain and growth in treated rats.

The fact that all animals could not be maintained for the duration of treatment was probably due to inadequate dosage, but difficulties in acquiring large amounts of progesterone prevented tests at higher levels. The dose necessary for the maintenance of a 50 g rat is about the same as that needed for a 700-1000 g ferret. This need for high dosage in the rat probably accounts for the many previous failures to notice the cortical hormone-like action of the luteal hormone[2]

Water Intoxication Studies. The sex hormones and the adrenal cortical hormones affect electrolyte and water metabolism of intact animals somewhat similarly (Thorn and Harrop and others[3, 4, 2]). One manifestation of an irregular electrolyte and water metabolism in adrenalectomized animals lies in their sensitivity to excess water, to which they react by the rapid appearance of "water intoxication" symptoms and death.[5, 6] These symptoms can be prevented by cortical hormone or salt.[5]

In view of the above facts we thought that some of the sex hormones, particularly progesterone, would probably modify the response to excess water, at least in adrenalectomized animals. Surprisingly, they had no effect either in normal or adrenalectomized rats, as seen from Table II. Experiments were conducted as previously described.[6] The rate of excretion of the water which had been administered by stomach tube, and the clinical symptoms were

3 Thorn, G. W., and Harrop, G. A., *Science*, 1937, **86**, 40.

4 Thorn, G. W., and Engel, L. L., *J. Exp. Med.*, 1938, **68**, 299.

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

6 Gaunt, R., Remington, J. W., and Schweizer, M., *Am. J. Physiol.*, 1937, **120**, 532.

TABLE I.
Survival of Progesterone-treated, Adrenalectomized Rats.

	No. rats used	No. died during treatment	Avg survival and range of rats dying on treatment	No. lived throughout treatment	Avg survival after treatment stopped	Avg max. wt gain	Avg wt diff. between operation and death	No. surviving indefinitely
			Series I.					
			Days		Days	g	g	
Progesterone-treated	12	7	9.7 (3-18)	5	7	17.7	+11.6	1
Controls untreated	14	14	6.0 (3-20)	—	—	3.4	+ 0.4	0
			Series II.					
Progesterone-treated	7	3	12.0 (9-16)	4	16	23.1	+20.0	0
Controls untreated	8	8	10.0 (8-15)	—	—	5.0	+ 3.0	0

TABLE II.
Response to Excess Doses of Water.

No. Rats used	Treatment	Water dosage	Avg % H_2O excreted at 7 hr	Avg % H_2O excreted at 11 hr	No. convulsive or prostrated	No. dying in 24 hr
6	Intact—Untreated	.06 cc/g* x 6 hr	84.8	92.9	0	0
6	Intact—3,333 I.U. amniotin-in-oil	,,	68.4	89.3	1	0
12	Intact—Untreated	.07 cc/g x 6 hr	71.5	83.5	4	1
6	Intact—3,333 I.U. amniotin-in-oil	,,	61.3	83.6	0	0
6	Intact—400 I.U. theelin-in-H_2O	,,	70.7	90.3	0	0
19	Adrex.†—Untreated	.06 cc/g x 5 hr	30.0	37.5	11	11
14	Adrex.—433 I.U. theelin-in-H_2O	,,	22.5	34.7	9	9
19	Adrex.—5 mg testosterone in propylene glycol	,,	15.0	20.7	16	16
9	Adrex.—Propylene glycol (1.0 cc)	,,	11.5	16.0	7	6
6	Intact—Propylene glycol (2.0 cc)	.07 cc/g x 6 hr	44.4	65.9	2	0
11	Adrex.—Progesterone (7.5 mg)	.06 cc/g x 5 hr	36.4	39.0	8	7
6	Adrex.—Cortical extract (4.0 cc)	,,	80.0	89.8	2	0
6	Adrex.—Normal saline (4.0 cc)	,,	35.5	48.5	1	1

*Six hourly doses of 0.06 cc H_2O per g body wt.
†Adrenalectomized.

the criteria observed. Hormones in oil (Amniotin, progesterone) were injected in divided doses, the first 36 hours before the experiment was begun, and the last 1-5 hours before its beginning. Injections of theelin-in-water and testosterone in propylene glycol were started 12-18 hours before the test and the last injections given during the first hours of water administration. In one experiment 5 mg of crystalline progesterone was flushed into the peritoneal cavity in saline suspension 12 hours prior to the experiment, in addition to injections of the hormone in oil. Cortical hormone was given an hour before and during the experiment. The cortical extract used was made up in normal saline, but its effects were largely due to the hormone and not the salt as seen by comparison of hormone and saline treated groups. Adrenalectomy was done 12 hours before the experiments started.

As seen from Table II none of the hormones given, except cortical hormone, modified the response in any significant way from that of comparable controls. Propylene glycol was a slightly deleterious agent, but testosterone dissolved in it did not vary its effect. The characteristic inability of the adrenalectomized rat to eliminate excess quantities of water in the absence of cortical hormone or salt was in no way compensated for by the sex hormones. This was particularly surprising for progesterone, since this substance will keep most adrenalectomized animals alive, and indicates either a qualitative difference between cortical extract and corpus luteum hormone action, or at least a difference in the rate of that action. It is possible that progesterone must be converted into some other chemical form to exhibit cortical properties.

Summary. Progesterone in doses of 1-2 mg per day extended the lives of young adrenalectomized rats in half of the cases throughout a 20-day treatment period. On the basis of equivalent dosage, it was much less effective than in adrenalectomized ferrets. Unlike cortical hormone, neither progesterone, estrin nor testosterone modified the response of adrenalectomized rats to excess water.