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Received December 29, 1958. P.S.E.B.M., 1959, v100.

Effect of Estrogen on Liver Glycogen in Adrenalectomized Rats.* (25654)

DWIGHT J. INGLE

Ben May Laboratory for Cancer Research, University of Chicago, Ill.

Large doses of injected estrogen cause increased glycogen in livers of intact fasting rats but not in livers of untreated adrenalectomized rats(1,2). It was concluded that the glycogenic activity of estrogen is mediated by increased secretory activity of the adrenal cortex. The present study demonstrated an extra-adrenal effect of estrogen upon level of glycogen in livers of adrenalectomized rats treated with adrenal cortical extract (ACE).

Methods. Male rats of the Sprague-Dawley strain weighing approximately 300 g were adapted to a medium carbohydrate diet(3), tube-fed each morning and late afternoon. The temperature was 74° to 78°F. Adrenalectomies and sham adrenalectomies were done by sterile technic under ether anesthesia. The adrenalectomized rats were treated with ACE (Upjohn) having glycogenic potency of 0.1 mg of hydrocortisone/cc. Whole adrenal cortical extract was used because it represents more complete replacement therapy than any single steroid. From fifth postoperative day, estradiol cyclophentyl-propionate (Upjohn) in oil solution (1 mg/cc) was injected subcutaneously in 0.1 mg daily for 4 days. Each rat was then fasted 24 hours and, under sodium cyclopal anesthesia, the liver was rapildly excised, weighed, and dropped into hot KOH. Glycogen was determined by the anthrone method(4). Since each rat had the same initial weight and was given the same amount of food, the results are expressed as total amount of liver glycogen/rat.

Results. Five experimental groups of 60 rats each were studied in relationship to dose of ACE given the adrenalectomized rats. Each group was divided into 4 equal subgroups: adrenalectomized, no estrogen; adrenalectomized, estrogen; adrenals intact, no estrogen; and, adrenals intact, estrogen. Each subgroup was equally represented in time. The values on liver glycogen are in Table I. Livers of rats treated with estrogen averaged 21% heavier than livers of rats not given estrogen. The average amount of glycogen recovered from liver varied somewhat, but in the non-adrenalectomized rat treated with estrogen a significantly greater amount was always found. Among rats not given estrogen, the average amount of liver glycogen in adrenalectomized rats was less than in intact rats until 6 cc of ACE/rat/day were given. The injection of estrogen was associated with increased liver glycogen in each subgroup of adrenalectomized rats, the amount increasing as dose of ACE was increased. Even with a dose of 6 cc of ACE daily, the adrenalectomized rats given estrogen showed significantly smaller amounts of liver glycogen than did the non-adrenalectomized rats given estrogen.

Discussion. Estrogen has an extra-adrenal effect on amount of liver glycogen in the rat. The mechanism of this effect is unknown. It is possible than increased secretion of cortical hormones by the estrogen-treated intact rat

* This research was supported by grant from Eli Lilly Co., Indianapolis, Ind.

TABLE I. Effect of Estradiol on Liver Glycogen in Intact Rats and in Adrenalectomized Rats Treated with Adrenal Cortex Extract. Fifteen rats/group.

ACE, cc/day	Adrenalectomy Liver glycogen, mg/rat No estrogen	Adrenalectomy Liver glycogen, mg/rat Estrogen	Adrenals intact, no ACE Liver glycogen, mg/rat No estrogen	Adrenals intact, no ACE Liver glycogen, mg/rat Estrogen
1	9.5 ± .52	12.3 ± .21	16.6 ± 2.11	105.3 ± 8.30
2	8.7 ± .71	35.0 ± 3.27	20.5 ± 2.97	76.6 ± 6.23
4	9.5 ± .95	39.7 ± 3.07	16.6 ± 1.88	89.0 ± 6.41
5	13.4 ± .76	51.1 ± 4.44	18.2 ± 1.76	72.3 ± 5.08
6	28.4 ± 4.37	62.4 ± 5.11	19.7 ± 2.31	93.8 ± 7.20

enhances deposition of liver glycogen: response to estrogen was greater in the presence of adrenals. It is also possible that estrogen has no glycogenic effect of its own but causes a rise in titer of cortical hormones by suppressing rate of destruction of these steroids. Mills(5) has published evidence that such can occur.

The principal effect of the cortical hormones in supporting the glycogenic effect of estrogen may be a permissive one. The term "permissive" was first used to call attention to biological responses which fail to become overt in the adrenally insufficient animal but do occur in adrenalectomized animals maintained in a state of eucorticalism by a steady intake of cortical hormones. It is assumed that the permissive role of a hormone represents normalizing the functions of organs—sustaining the integrity of metabolic processes and thereby the capacity to adapt and respond. A large number of biological responses are now known to require the presence of cortical hormones but not the adrenal glands. The term "permissive," although still useful, covers our ignorance of several mechanisms by which hormones and other biological principles support homeostasis and adaptability.

Summary. Among 300 force-fed male rats of the Sprague-Dawley strain (300 g initial wt.), estrogen increased liver glycogen in the fasting adrenalectomized rat treated with ACE whereas this effect was not observed in the adrenally insufficient animal. The glycogenic effect of estrogen was greater in intact rats than in adrenalectomized rats treated with ACE.

Acknowledgement is made of the technical assistance of Mr. Mitchell Heller and Mr. Melvin Vinik on some experiments.

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Received January 29, 1959. P.S.E.B.M., 1959, v100.

Effect of Dietary Iron on Phosphate Metabolism.* (24655)

WOLFGANG BUTTNER† AND JOSEPH C. MUHLER
Dept. of Biochemistry, Indiana University Medical Center, Indianapolis

In experiments involving the effect of different carbohydrates on the calcification process, differences were observed that could not be accounted for by any readily known mechanism. Upon further scrutiny of the dietary components as well as the experimental procedures, it was found that the mineral supplement used in these studies had an unusually large iron content. This observation prompted us to design a study in which the amount of

* This study was supported in part by grant from Procter and Gamble Co., Cincinnati, O.

† Post-doctorate fellow. Present address: Univ. of Mainz, Germany.