

which has been reported to have a half-life longer than that of hydrocortisone. Others studied include tetrahydro-hydrocortisone, 20-hydroxy-hydrocortisone, cortisone, and corticosterone(8,9); each of these has a half-life shorter than that of hydrocortisone. Of the steroids mentioned only cortisone, hydrocortisone, and Δ^1 -hydrocortisone have a Δ^4 -17, 21-dihydroxy-3,20-keto configuration and are potent glucocorticoids. Among these 3, the glucocorticoid potency and the half-life are related in such a way as to suggest that glucocorticoid potency is inversely proportional to the rate of metabolism.

Summary. The influence of oral or intravenous administration of Δ^1 -hydrocortisone on plasma 17-OHCS concentrations was studied. With comparable oral doses Δ^1 -hydrocortisone produced 17-OHCS elevations of greater magnitude and longer duration than did hydrocortisone. Also, the half-life of the Δ^1 -steroid was longer than that of hydrocortisone. It was concluded that a slower metabolism of the Δ^1 form occurs and postulated that this might contribute to the greater clinical effectiveness of this steroid.

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A Non-hypophyseal Sex Difference in Estrous Behaviour of Mice Bearing Pituitary Grafts.* (22308)

CARLOS MARTINEZ AND JOHN J. BITTNER.

Department of Physiology, Division of Cancer Biology, University of Minnesota, Medical School, Minneapolis.

Differences in size of the pituitary gland related to sex have been described in some species, the female gland being larger and heavier than that of the male. Similarly, the gonadotrophic potency of injected hypophyseal extracts from males is greater than those prepared from female pituitaries(1,2). Castrated male guinea pigs with grafted ovaries showed a greater stimulation of the mammary glands and other sexual structures, than intact females(6). The same was true in castrated male mice bearing ovarian and vaginal grafts.

There was a continuous non-cyclic stimulation of the vaginal tissue(5). However, Harris and Jacobson(3,4) have demonstrated that hypophysectomized female rats bearing male hypophyseal grafts from newborn donors, had normal estrous cycles, became pregnant and delivered their young at term. This would indicate that the characteristic cyclic gonadal function of the female, as compared to the non-cyclic of the male, would not be related to the sex of the pituitary, but rather to a sex difference in some other structure. Since functional pituitary grafts can be placed in hypophysectomized mice by means of a rather simple one-stage operation, we have

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used this animal preparation to investigate further the problem of estrous behaviour in hypophysectomized females and males bearing either male or female hypophyseal grafts, respectively.

Material and methods. Young mice of both sexes of the Z (C3H) stock and AZF₁ hybrids (A ♀ x Z ♂) were used. Hypophysectomy was performed according to the technic described by Thomas(7). The grafting of hypophyseal tissue was done as follows: The donor was killed by ether, the scalp and brain were lifted and the gland was removed and placed in a container with saline. Upon completion of hypophysectomy, the gland to be grafted was transferred to the emptied sella turcica of the host either with a fine pair of forceps or by holding the gland at the distal end of a very thin glass pipette by applying a slight negative pressure. The entire procedure was completed within 4 to 5 minutes and postoperative mortality did not exceed 10%. By this procedure, the overall incidence of successful hypophyseal grafts was 85% of a total of 325 operated animals for other studies. Mice bearing hypophyseal successful grafts have shown normal sexual activity throughout their lives (12 to 16 months). Two types of experiments were done. In one, the body weight changes were determined and the sexual cycles studied in 4 groups of female mice of the Z(C3H) strain, as follows: a) hypophysectomized; b) sham operated controls; c) hypophysectomized bearing a hypophyseal graft taken from a female donor of the same strain and age; d) hypophysectomized bearing a hypophyseal graft from a male donor of the same strain

and age. In all groups the body weight was determined before and at weekly intervals after the operation. Similarly vaginal smears by the douche technic were taken daily during 1 week, at monthly intervals to determine the presence or absence of estrous cycles in the different groups. In another experiment, 2 groups of male AZF₁ hybrid mice were used. One of them was submitted to hypophysectomy followed by the graft of one hypophysis taken from a female donor. Another group carried their own (male) hypophysis. Three weeks after the operation, both groups of mice were castrated and 2 ovaries and a ring of vaginal tissue taken from female mice of the same strain and age were grafted subcutaneously, using the technic described by Huseby and Bittner(5). Finally, after a period of one month following the vaginal transplant, mice were killed, the grafts removed and studied histologically. The presence of hyperplasia and hypertrophy of the epithelial wall of the vaginal graft, and a complete cornification of the content of the lumen, without signs of cyclic activity, was interpreted as indicative of a continuous estrogenization(5).

Results. The results obtained in the first experiment, in which only animals showing successful takes of the grafts were included, are listed in Table I and can be summarized as follows: a) Sham hypophysectomized controls showed a progressive increase in body weight after the operation and, as was expected, normal estrous cycles. b) Hypophysectomized alone showed a progressive decrease in body weight and absence of estrous cycles. c) In both groups of hypophysecto-

TABLE I. Effect of Sex of Pituitary Gland Grafted into Hypophysectomized Female Mice on Body Weight and on Estrous Cycles.

Group	No. of mice	Body wt in g (mean)			Presence of estrous cycles*
		Before operation	1 mo after	2 mo after	
Sham operated controls	15	16.50 ± .38	19.25 ± .39	22.90 ± .42	Yes 15/15
Hypophysect. bearing ♀ pituitaries	15	15.91 ± .41	17.62 ± .44	18.94 ± .39	" 15/15
Hypophysect. bearing ♂ pituitaries	22	16.20 ± .36	17.90 ± .34	19.05 ± .28	" 22/22
Hypophysectomized	12	16.80 ± .45	15.10 ± .50	15.00 ± .49	No 12/12

* Normal estrous cycles in animals bearing pituitary grafts appeared at 10 to 15 days following operation.

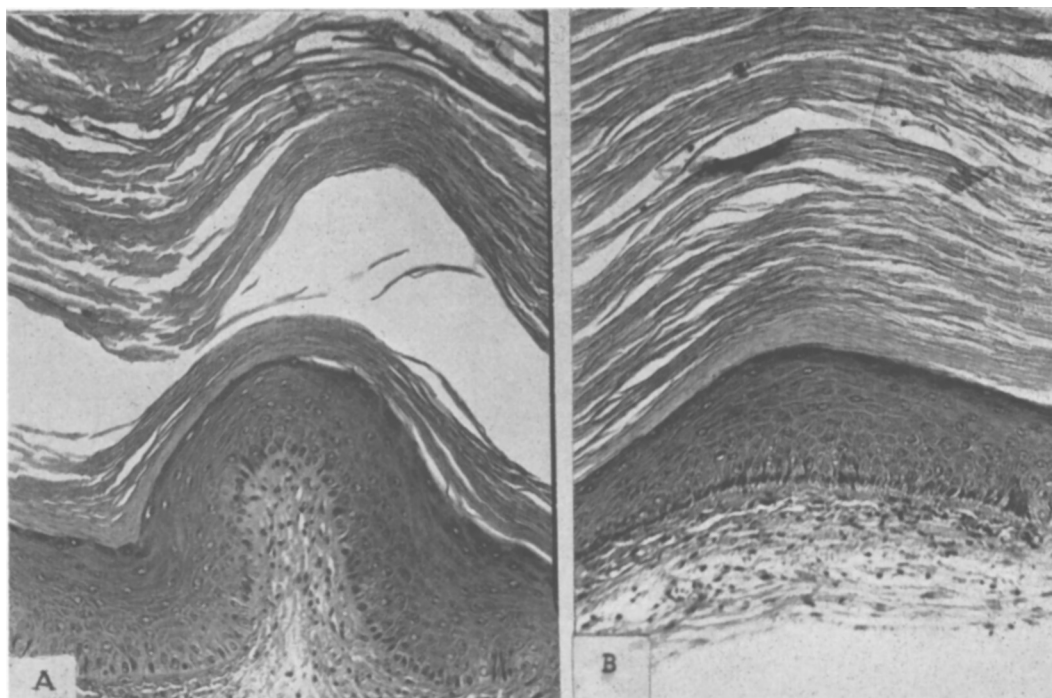


FIG. 1. Histological sections taken from vaginal grafts in castrated male mice with grafted ovaries, bearing either a female (A) or a male (B) hypophysis.

mized females bearing either a female or male hypophyseal gland, progressive increase in body weight and normal estrous cycles were observed.

Table II shows the results of the second experiment. Both groups of castrated males with grafted ovaries showed the typical non-cycling vaginal reaction characteristic of a continuous estrogenization, regardless of the sex of the pituitary gland grafted (Fig. 1).

Discussion. From the results described, it seems clear that hypophysectomized female mice bearing either female or male pituitaries had normal estrous cycles. These results agree with those obtained by Harris and

Jacobson(3,4) in the rat. Furthermore, castrated male mice with grafted ovaries showed a continuous noncyclic vaginal stimulation regardless of the sex (female or male) of the hypophyseal tissue grafted.

These results would imply that the normal cyclic function of the female pituitary as opposed to the non-cyclic of the male, as it was formerly described, would not reside in a sex difference of the hypophyseal tissue in itself, for in our experiments, the property of cycling or non-cycling seemed to be determined by the sex of the host, rather than that of the pituitary gland they carried.

In the light of these data it is rather difficult to decide as to where and how the sex difference in gonadal function of the hypophysis originates. Not being involved, as it appears, the sex of the hypophyseal gland, and since anatomically this organ is related to the hypothalamus in the brain through vascular and nervous connections, it would be perhaps justified to assume that the cyclic or non-cyclic character of the female or male gonadotrophic function might depend upon a

TABLE II. Effect of Sex of Pituitary Gland on Development of Vaginal Grafts in Castrated Males with Grafted Ovaries.

Group	Pituitary	No. of mice	Histology of vaginal grafts
Castrated with grafted ovaries	♂ (own)	10	Cornified non-cyclic 10/10
<i>Idem</i>	♀	8	<i>Idem</i>
"	None	2	Atrophic or reabsorbed

sex difference of that nervous structure.

Summary. Estrous behaviour in hypophysectomized female and male mice bearing hypophyseal grafts has been studied. The results were: (1) Hypophysectomized female mice bearing either female or male hypophyseal grafts, showed complete and normal estrous cycles. (2) Castrated males bearing ovarian and vaginal grafts showed a continuous noncyclic type of vaginal stimulation regardless of whether they had been grafted with male or female pituitaries. (3) The characteristic cyclic function of the female hypophysis may be related to the cyclic function of some other controlling structure rather

than being dependent upon the pituitary gland itself.

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Threshold of the Enterogastric Reflex.* (22309)

EDWARD R. WOODWARD[†] AND HERBERT SCHAPIRO.

Department of Surgery, University of California Medical Center, and Wadsworth General Hospital, Veterans Administration Center, Los Angeles, Calif.

Introduction of acid into the duodenum causes a prompt and complete inhibition of gastric motility. This phenomenon has been named by Thomas, *et al.*, the "enterogastric reflex"(1). In a previous study, we reported this inhibition in the human subject and found that it occurred in patients with vagotomy, extensive sympathectomy, partial gastric resection, and spinal cord transection(2). It is the purpose of the present study to explore the threshold of this inhibitory mechanism and to determine its presence in patients with gastric achlorhydria.

Method. As previously described(2), a duodenal tube was passed under fluoroscopic control. A second tube with an attached balloon was passed into the antral portion of the stomach, and gastric motility was recorded. Studies were performed on 11 normal human subjects, varying both the volume and concentration of hydrochloric acid solutions instilled via the duodenal tube. In most pa-

tients, 2 or more determinations were made during the same study period—a total of 25 studies. In addition, the same study was performed on 3 patients with persistent gastric achlorhydria as determined by histamine stimulation.

Results. 1. *0.075 N HCl:* In 4 patients, 100 cc of 0.075 N HCl introduced into the duodenum caused a prompt inhibition of gastric motility varying from 26 to 39 minutes. Twenty-five cubic centimeters of the same solution in one patient caused only a 10 minute period of inhibition. 2. *0.05 N HCl:* One hundred cubic centimeters of 0.05 N HCl infused into the duodenum of 5 subjects resulted in cessation of gastric motor activity varying from 9 to 26 minutes. In 2 patients, 25 cc of the same solution instilled into the duodenum caused a 5 and a 6 minute inhibition, respectively. 3. *0.025 N HCl:* One hundred cubic centimeters of 0.025 N HCl was introduced into the duodenum of 3 subjects and was immediately followed by inhibition of gastric motility lasting for 9 to 16 minutes. In 1 patient, 25 cc of this solution produced a 10-minute period of inhibi-

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[†] John and Mary R. Markle Scholar in Medical Science.